Federated learning approaches for fuzzy cognitive maps to support clinical decision-making in dengue

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Abstract

Federated learning is a distributed machine learning approach developed to guarantee the privacy and security of data stored on local devices. In healthcare, specifically in diseases of public health interest such as dengue, it is necessary to develop strategies that guarantee such data properties. Therefore, the aim of this work was to develop three federated learning approaches for fuzzy cognitive maps for the prediction of mortality and the prescription of treatment of severe dengue. The validation of the approaches was performed on severe dengue datasets from two dengue endemic regions in Colombia. According to the results, the use of federated learning significantly improves the performance of models developed in centralized environments. Additionally, the use of federated learning allows guaranteeing the privacy and security of each client's data due to the local training of the models. Federated learning is a useful tool in healthcare because it guarantees the privacy and security of patient data. Our results demonstrated the ability of aggregated models to predict mortality and prescribe treatment for severe dengue.

Keywords: Fuzzy cognitive maps, Federated learning, Clinical decision-making, Predictive modeling, Prescriptive modeling

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1. Introduction

Dengue is a febrile disease caused by a virus of the *Flaviviridae* family, and is transmitted by the bite of female *Aedes* mosquitoes [1]. It causes a clinical picture ranging from asymptomatic processes to severe disease; with a wide spectrum of clinical manifestations such as fever, headache, retro-ocular pain to severe signs such as shock, severe bleeding, multi-organ failure and death [2]. Based on severity, World Health Organization (WHO) categorized the disease into three: i) dengue without alarm signs, ii) dengue with alarm signs, and iii) severe dengue (SD), which includes dengue shock syndrome [3]. The latter category is an important cause of mortality and has reached a rate of 44% [4]. Dengue infection has spread globally, being endemic in more than 120 countries worldwide, mainly in Africa, Western Pacific, Southeast Asia and the Americas, generating a high epidemiological, economic and social impact [5]. According to the WHO, more than 3.8 billion people are at risk of infection and approximately 100 to 400 million infections occur annually worldwide, with approximately 25% of them showing some type of symptom [6].

Diagnosis and treatment of dengue are the main components of the clinical management of the disease. Diagnosis is made by interpreting signs and symptoms to classify the patient according to the severity of the clinical picture, which can be challenging for health personnel due to the variability of clinical manifestations present in infected patients. Additionally, dengue presents similar clinical manifestations to other febrile diseases such as Zika, chikungunya and leptospirosis, with which a differential diagnosis should be made [7]. On the other hand, laboratory tests such as detection of dengue antigens, antibodies against the virus and viral isolates, allow confirmation of the disease, but may cause delays in areas that do not have all the health services [8]. There is currently no specific antiretroviral treatment for dengue available in developing countries. Therefore, available treatment focuses on alleviating signs and symptoms and avoiding complications leading to death, and clinical management of dengue remains a challenge for health professionals [9].

One way to address the problem of clinical management is through the development of computer-aided approaches that use predictive modeling for diagnosis and prescriptive modeling for treatment. The development of such methods can support medical decision-making in relation to the course of disease, which could have an impact on reducing mortality rates due to timely classification and appropriate treatment [10].

The validation of models, approaches and methodologies for the diagnosis and treatment of dengue is quite widespread. However, the works reported in the literature present some limitations. First, the published studies focus on developing complex models that are not very understandable for the medical professional, who is interested in knowing how the model classifies patients according to their severity. Moreover, they maximize predictive performance by compromising the interpretability of predictor variables in different situations or scenarios. Second, there are few studies focused on the clinical management of dengue in a comprehensive manner. Most of the studies only emphasize one of the two components: diagnosis or treatment; however, it is crucial to integrate both processes to optimize medical decision-making aimed at improving health care. Third, the reported works use the traditional machine learning (ML) approach, which gathers dengue data in one place for training. This may raise issues with respect to the privacy and security of the data used. Transporting and sending the data from one place to another can cause loss, damage and violate laws related to personal data protection.

Therefore, it would be of great clinical utility to generate decision support approaches for the diagnosis and treatment of dengue that provide understandable and explainable results for clinicians. It would also be of clinical interest to develop systems that, in addition to predicting an outcome, also allow treatment to be prescribed according to the specific patient scenario. Finally, the use of distributed learning approaches such as federated learning that guarantee data security and privacy would be a great added value.

In this sense, the main contributions of our work are the definition of three approaches as medical support tools for the diagnosis and treatment of dengue, specifically SD. These approaches are characterized by using federated learning with fuzzy cognitive maps (FCMs) and optimization algorithms for the generation of predictive and prescriptive models. The first approach implemented is based on the similarity of the feature space among the participating clients or sites where the signs and treatment options of SD are identical. The second is based on the objective, where the only feature in common among all clients or parties is a decision variable (for our application domain, it was SD mortality). Each client or party has different characteristics related to mortality and treatment of SD. Finally, the third approach uses parameter learning transfer to send information from one site/party to another. Specifically, the implemented approach transmits the learned parameters from SD treatment to mortality prediction. The novelties proposed in the present study are focused on several aspects: i) the generation of federated learning approaches with a different architecture (approaches 1 and 2) from that reported in the literature; ii) 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; iii) the combination of predictive and prescriptive models in a single architecture that allows integrated support for decision-making with respect to the diagnosis and treatment of dengue.

This paper is organized as follows: Section 2 shows the related works about the last trends in FCMs for prediction and prescription. Also, it presents the main studies about federated learning for medical environments. Section 3 describes the methodology used to develop the federated learning approaches, and Section 4 describes the experiments to validate them. Section 5 shows the results for each approach and discusses them. Finally, Section 6 concludes the paper.

2. Related work

In this section, we present the main works related to the use of FCMs for prediction and prescription. Additionally, we present the main studies about federated learning for healthcare.

2.1. FCMs

FCMs are computational intelligence algorithms that allow modeling complex systems using concepts and relationships between them [11, 12]. In the following, we present a literature review on the implementation of this type of algorithm for prediction and prescription.

2.1.1. FCMs for prediction

FCMs use inference functions to make predictions based on the interconnection among the concepts [13]. The development of clinical decision support systems for prediction with FCMs has increased in recent years due to the simplicity of construction and ease of interpretation of results. In previous work, we developed a clinical decision support system for dengue diagnosis based on FCMs [14]. We used the knowledge and experience of clinical experts in dengue to construct the FCM with signs, symptoms, and laboratory test results. The constructed FCM model had the ability to classify dengue severity (dengue with and without warning signs, and SD) with 89% accuracy and the additional ability to assess the behavior of severity-related variables. In addition, we developed another previous work with SD prediction models using FCMs trained with the particle swarm optimization algorithm [15]. The models were trained using historical data from two endemic cities in Colombia and their peak performance reached 74% accuracy due to small sample sizes.

FCMs have also been widely used for predicting the risk of outbreaks or epidemics of viral diseases such as dengue [16, 17]. For example, Pelaez [16] proposed a model based on FCMs to predict the risk of presenting tropical viral diseases such as dengue. The authors trained FCMs with unsupervised learning to represent causal relationships and knowledge related to environmental conditions, symptoms, and historical data related to tropical viral diseases. The historical data for training the FCMs corresponded to seasonal outbreaks and epidemics in Ecuador. The proposed model had the potential to improve the chances of early forecasting of seasonal diseases related to tropical regions. Jayashree et al [17] used FCMs using expert knowledge to build a system that classified the risk of dengue outbreak in tropical regions of Southern India. The results showed that the performance of FCM was superior when compared to other techniques such as Bayesian classifier, decision tree, support vector machines, and multilayer perceptron. The classification of risk into low, moderate and high allows health authorities to establish prevention strategies in the regions to prevent the spread of the disease.

2.1.2. FCMs for prescription

FCMs have now started to be used to prescribe actions leading to desired outcomes in complex modeled systems. Reported work in the literature using FCMs to support decision-making related to dengue treatment is scarce. However, they have been used for the treatment of other diseases such as urinary tract infections and cancer. Papageorgiou [18] developed a computational tool based on FCMs for treatment management of urinary tract infections. The results of the evaluation of the software on a small sample of diseased patients demonstrated its capability for classification and recommendation of suggested treatments.

For cancer treatment, several studies have been performed for treatment management using radiotherapy [19, 20]. Papageorgiou [19] used FCMs for computational modeling of the complexity of the clinical radiation procedure to calculate the final dose that should be administered in cancer patients. The model was built with a combination of expert knowledge and fuzzy rule extraction from the data. The system was able to handle uncertainty, is simple, and is less complex than other previously reported models. Papageorgiou and Stylios [20] determined the success of the radiation therapy process by implementing FCMs as a modeling technique. The proposed system had a hierarchical structure to simulate and evaluate the radiation therapy process. The developed model was evaluated in point scenarios to demonstrate its performance with prior determination of treatment variables by the medical professional.

According to our literature review, only one work has used FCMs for dengue treatment prescription. Hoyos et al [15] developed an extension of FCMs with optimization algorithms for the generation of prescriptive models. The proposed algorithm uses a genetic algorithm to optimize prescriptive variables leading to desired system values. The methodology was tested in the treatment of SD. The evaluation of the generated model showed a good performance yielding accuracies between 81% and 100% accuracy for recommending treatment options for SD, which constitutes an excellent tool to support decision-making for the treatment of SD and reduce mortality rates.

2.2. Federated learning in medical environments

Federated learning is a distributed ML approach developed by Google [21]. This approach allows training models with distributed data anywhere in the world, such that local models are trained with their data and its parameters are shared in a federated server to build a global model. The main feature of this approach is that the data never leave their original location. This type of methodology is useful to attack the problem of guaranteeing data security and privacy, mainly, in clinical environments [22]. Federated learning in recent years has attracted the attention of the scientific community due to its interesting ability to generate global models avoiding data sharing between involved parties [23]. This distributed ML approach has been widely used in healthcare due to the security and privacy of data in this domain. Additionally, this approach can be used to transfer learning from one healthcare institution to another [24].

Several surveys and literature reviews have provided comprehensive reviews of the work reported in the literature on architectures, approaches, use, and application of federated learning for healthcare [25–28]. For example, Antunes et al [25] present a systematic literature review where they discuss the main problems of federated learning, possible solutions and the most frequently used ML methods. Additionally, they propose an architecture based on the results of the systematic review. A survey by Nguyen et al [26] presents the main advances and requirements for a correct implementation of federated learning with the internet of medical things. The authors review several current researches and analyze different aspects such as medical imaging, remote health monitoring and data management. Prayitno et al [27] provide a systematic review of current advances in federated learning for healthcare applications with a data-centric perspective. The review evaluates the use of reference datasets, data protection strategies, data partitioning and distribution properties. Finally, Xu et al [28] conducted a survey presenting a general review on federated learning, specifically, issues related to data privacy, system challenges, and possible solutions to statistical challenges in implementing federated learning in medical environments.

According to our literature review, there are no papers that have implemented federated learning for dengue analysis. However, different works on federated learning have been reported for other events of interest in public health. This type of work can be classified into two main groups based on the types of data used: i) federated training for unstructured data, mainly the use of biomedical images; and ii) federated training for structured data. In the following, we will show some relevant works developed in each group.

2.2.1. Federated learning for unstructured data

Unstructured data are those that do not have a defined structure. Within this group, we find images, text and audio. In clinical environments, the most commonly used data type to implement federated learning approaches are medical images such as X-ray images, CT scans, nuclear magnetic resonance and histopathological images. Thus, several works have been developed to detect COVID from chest X-ray images [29], brain tumor detection [30], and histopathological image analysis [31]. Feki et al [29] proposed a federated collaborative learning approach with deep learning for COVID-19 screening in several healthcare institutions without sharing data among them. The authors used two pre-trained convolutional neural network architectures, VGG16 and ResNet50. The accuracy of the models in the federated approach was similar for both VGG16 and ResNet50 when compared to the centralized approach. Sheller et al [30] compared a federated learning approach with collaborative data sharing learning. The study was conducted across several institutions storing brain tumor images. The models developed with federated learning were able to achieve superior performance to the data sharing approach with the additional value of ensuring privacy and confidentiality of the data used. Adnan et al [31] proposed a differentially private federated learning approach for medical image analysis, specifically, histopathological images across multiple healthcare institutions. Although models with federated learning performed well, learning with centralized data obtained better accuracy values.

2.2.2. Federated learning for structured data

Structured data are those composed of data frames where the columns correspond to patient variables or characteristics and the rows represent the records of each patient. This type of data has been widely used in building federated learning approaches and models [32–36]. For example, Brisimi et al [32] developed an algorithm to generate federated predictive models with sparse Support Vector Machine to predict hospitalizations due to cardiac diseases. The results showed the ability of federation to generate a global model with local models trained on several hospitals, however, the global model did not perform superior to the local models. Dang et al [33] implemented mortality prediction models in intensive care units of several hospitals in a federated environment using two aggregation algorithms (FedAvg and FedProx) and two training approaches (local and centralized). Of all the approaches implemented, FedProx performed the best, however, there was no significant difference between centralized training and federated training. Rahman et al [34] developed regression models in a federated environment to predict the length of hospital stay of patients in ten hospitals. The models were evaluated and the results showed that the performance of the models increases when the number of aggregated clients in the federated server increases. Kerkouche et al [35] proposed a federated learning approach that preserves data privacy for the prediction of in-hospital mortality. The authors found a relationship between model performance and patient-level privacy. Increasing the level of privacy decreases prediction accuracy. Finally, Salmeron & Arevalo [36] developed an approach based on FCMs for breast cancer diagnosis, and additionally, preserve data privacy. The development of this approach allowed obtaining performance of federated global models superior to the local models and the model trained with centralized data.

3. Methodology

In this section, we describe the general methodology of the present study. First, we show a global workflow where we schematically represent the activities performed in our research for the development of models under the federated approach and the traditional ML approach. Then, we present the techniques used to build the predictive models (data-driven PSO-FCM) and prescriptive models (PRV-FCM). Finally, we describe the federated learning approaches reported in the literature and the proposed approaches. Fig. 1 shows a schematic representing the workflow of this research. Initially, 80% of the data is used for training and validation of the models. We use 5-fold cross-validation to tune hyperparameters and select the best predictive and prescriptive models. The evaluation of these models was done with the remaining 20% of the data. Specifically, for the proposed federated approaches, predictive and prescriptive models are trained and tested on local datasets. The parameters of these models are aggregated to build a global model. For the traditional approach, the data were pooled to obtain a single dataset to perform training and testing on the corresponding data. At the end, we performed a comparison of all the predictive and prescriptive models obtained.

3.1. Data-driven PSO-FCM

Predictive models were generated using FCMs due to their simplicity of construction, and inference and interpretability skills. An FCM is a computational intelligence technique that simulates human reasoning with concepts and relationships [11, 37]. Concepts correspond to variables within a system and relationships are the influence between those concepts. An FCM can be represented by a matrix that shows the relationships among the concepts. For example, Eq. 1 shows a

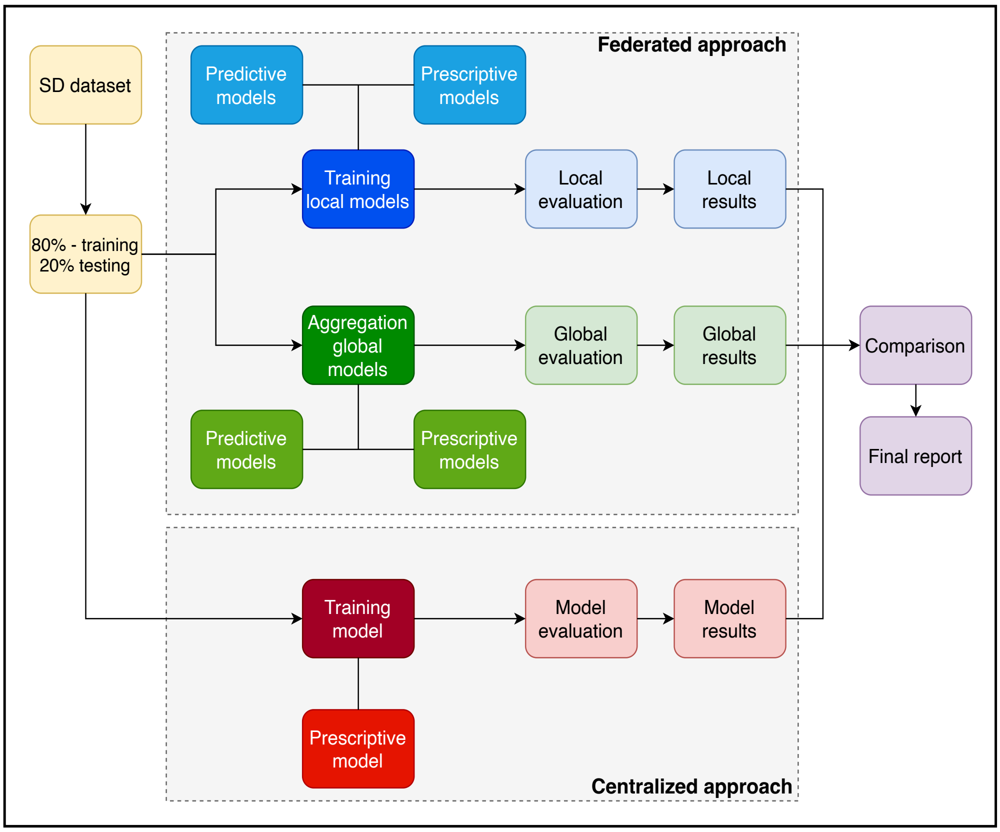

Fig. 1. Flowchart representing the main activities performed in this research.

matrix for five concepts and five relationships among them, represented by the values of w_{ij}. Fig. 2 shows a schematic representation of the FCM defined in the matrix of Eq. 1.

$$\mathbf{W} = \begin{array}{c} \\ \boldsymbol{C_1} \\ \boldsymbol{C_2} \\ \boldsymbol{C_3} \\ \boldsymbol{C_4} \\ \boldsymbol{C_5} \end{array} \begin{array}{c} \begin{array}{ccccc} \boldsymbol{C_1} & \boldsymbol{C_2} & \boldsymbol{C_3} & \boldsymbol{C_4} & \boldsymbol{C_5} \end{array} \\ \begin{pmatrix} 0 & 0 & 0 & 0 & w_{15} \\ 0 & 0 & 0 & 0 & w_{25} \\ 0 & w_{32} & 0 & 0 & w_{35} \\ 0 & 0 & 0 & 0 & w_{45} \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \end{array} \tag{1}$$

FCMs have been mainly used for description, prediction, and lately, they have been used for prescription. These three aspects are developed using inference rules that allow an initial state vector to reach a stable state. For the construction of the predictive models, we used the data-driven PSO-FCM technique. This technique uses the particle swarm optimization algorithm on

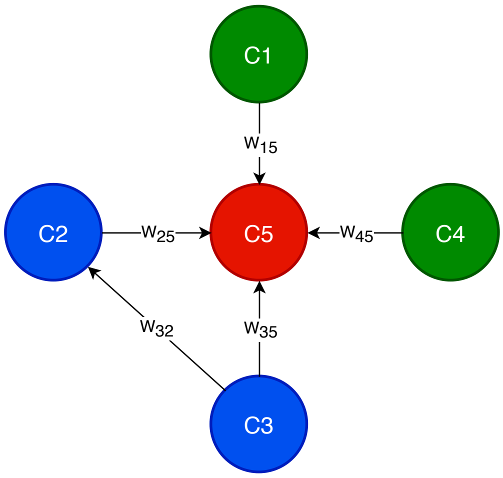

Fig. 2. Example of an FCM with five variables and five relationships.

datasets to find an FCM that describes relationships between the variables. The data-driven PSO-FCM algorithm is defined by:

$$v_i(t+1) = v_i(t) + s_1 r_1 \cdot (W_i^{best} - W_i(t)) + s_2 r_2 \cdot (W_i^{gbest} - W_i(t)) \quad (2)$$

$$W_i(t+1) = W_i(t) + v_i(t) \quad (3)$$

where v_i is the particle velocity; r_1 and r_2 are random values with uniform distribution; s_1 is the cognitive coefficient, responsible for the particle tending to move towards the position where it has obtained the best results so far; s_2 is the social component, also known as collective behavior, it is responsible for the particle tending to move towards the best position found by the swarm so far; W_i^{best} is the best position obtained by a specific particle, while W_i^{gbest} is the best position obtained by any particle in the swarm. For this case, each particle i is an FCM, while the position is a candidate matrix to build each FCM.

3.2. Prescriptive-FCM

The generation of prescriptive models was developed with the PRV-FCM methodology [38]. This methodology uses the inference process of FCMs and optimization algorithms to find optimal values of prescriptive variables that lead to the desired results to the concepts of the system. PRV-FCM first characterizes variables depending on their nature into prescriptive or action variables and system variables. Prescriptive variables are actions that a decision maker can perform to solve a problem, while system variables are those related to the system to be modeled. After initializing the system with desired values, an optimization algorithm is used to find the values of the prescriptive variables that lead to the desired values to the system variables.

3.3. Federated learning

Federated learning is a distributed ML approach developed in 2017 [21]. Federated learning allows to collaboratively generate a shared ML model by keeping all training data at its place of origin or collection, decoupling the ability to do ML from the need to store the data in the cloud. Federated learning works like this: one party downloads the current model, improves it by learning from local data, and then summarizes the changes as a small update. Only this model update is sent to the cloud, via encrypted communication, where it is immediately averaged with updates from other parties to improve the shared model. All training data remains in its original location, and no individual updates are stored in the cloud.

To date, three main approaches have been developed, known as horizontal federated learning, vertical federated learning, and federated learning with transfer learning. Fig. 3 shows a schematic representation of each. A brief explanation of each follows.

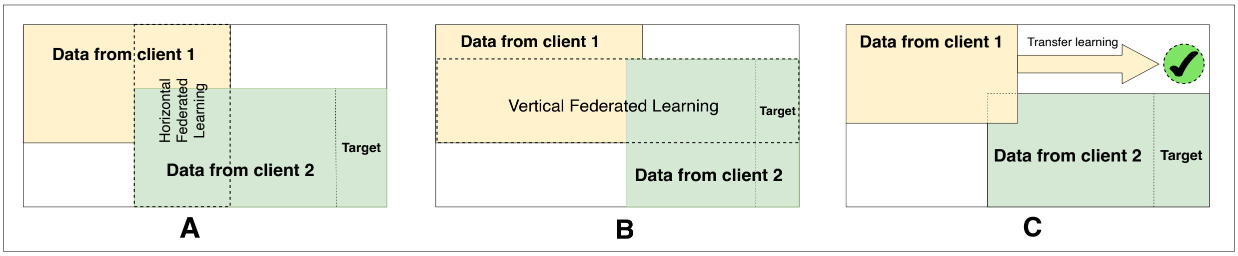

Fig. 3. Schematic representation of federated learning approaches reported in the literature. **A** y **B** represents horizontal and vertical federated learning, respectively, while **C** represents federated learning with transfer learning.

3.3.1. Horizontal federated learning

Scheme A in Fig. 3 shows horizontal federated learning. This type of federated learning is suitable in the case where the features/variables of the two datasets overlap a lot, but the records/data overlap little. Horizontal federated learning consists of splitting the datasets horizontally (by the dimension of the records), and then, extracting the part of the data where the features/variables are the same but the records are not exactly the same [39].

3.3.2. Vertical federated learning

Vertical federated learning is shown in Scheme B in Fig. 3. Vertical federated learning is suitable in the case where the features/variables of the two datasets overlap little, but the records/data overlap a lot. Vertical federated learning consists of splitting the datasets vertically (by the dimension of the features/variables), and then, extracting the part of the records that are the same, but the features or variables are not exactly the same [40].

3.3.3. Federated transfer learning

A representation of federated learning with transfer learning is shown in Scheme C in Fig. 3. In the case where the records and variables in the two datasets rarely overlap, the data is not segmented, but transfer learning is used to overcome the missing data or labels. In this approach, models are trained on one dataset and applied to another dataset from another related domain. [41].

3.4. Our proposed approaches

In this section, we describe each of our federated learning approaches. Fig. 4 shows schematic representations of each of the approaches.

3.4.1. Total federated FCM

Scheme A in Fig. 4 shows this approach. We call this approach *total federated learning* because all the variables in client 1 have the same characteristics/features as those in client 2. A clear example is all the signs, symptoms, laboratory tests and classification of dengue in different cities in Colombia.

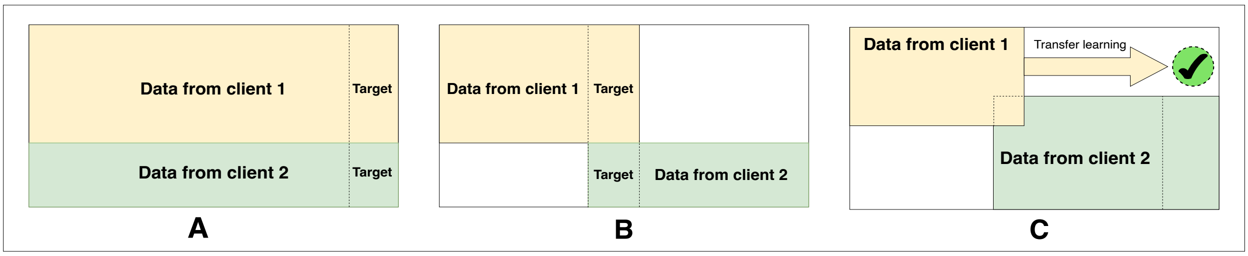

Fig. 4. Schematic representation of our federated learning approaches. **A** represents total federated learning; **B** represents target-based federated learning; and **C** represents federated learning with transfer learning.

For this case, the local models are trained by generating a weight matrix W_i^l, where i is the model number and l indicates that the model is local. Each local model sends the parameters to the server and this calculates an updated matrix by aggregating the information using the arithmetic average. Subsequently, the updated matrix W_{ij}^G is sent to each of the parties so that the updated model is used everywhere. The aggregation of the parts is performed with the average using the following equation:

$$W_{ij}^G = \frac{1}{n}\sum_{c=1}^{n} W_{ij}^c \tag{4}$$

Where W_{ij}^G is the global matrix aggregated with the two local model matrices, n is the number of clients used, and c is the client/site number.

3.5. *Federated target-based FCM*

In target-based federated learning, only one characteristic is common among the parties involved, and it corresponds to the target (see Scheme B in Fig. 4). This case is focused on predictive models. For example, one city has signs, another city symptoms, and finally, another city laboratory tests. In our problem, the only common variable is the label or target for the diagnosis or prediction of mortality due to SD. From that, a global model is constructed that includes all the variables from all the cities. Since in this case, there are no common concepts, simply the weights corresponding to the concepts of the different parts of the architecture are added. At the end, each city has a global model with all the characteristics to be used. The aggregation process is done according to the following equation:

$$W^G = \begin{bmatrix} 0 & W_{ij} \\ W_{kl} & 0 \end{bmatrix} \tag{5}$$

Where W^G is the global matrix, W_{ij} is the local matrix of local model 1, and W_{kl} is the local matrix of local model 2.

3.6. Federated FCM with transfer learning

The federated FCM with learning transfer is useful for the development of prescriptive models. Scheme C in Fig. 4 shows the design of this approach. For this variant, the concepts are divided into system and action. In one part are the action concepts that act on the system concepts. For example, treatment concepts that influence signs or symptoms. In another part are the system concepts that influence the prediction. The aggregation process is done using Eq. 5. In that particular case, the predictive model of the second party is previously trained/built, and then, it is transferred for the second party to use to build the predictive model.

4. Experiments

In this section, we describe the experiments to validate the proposed approaches. First, we describe the datasets used. Then, we show the statistical validation process using 5-fold cross-validation. Subsequently, we present the evaluation metrics, and finally, we present a brief description of the experimental setup for the generation of local and global models in each proposed approach.

4.1. Datasets

For the validation of our approaches, we used two datasets from two dengue endemic regions in Colombia: Medellín and Córdoba. According to data from the National Institute of Health, this municipality and department are endemic because of the dengue incidence rates they show annually of 161-745 and 51-503 per 100,000 inhabitants for Medellín and Córdoba, respectively [42]. The selected datasets correspond to dengue mortality. Dataset 1 corresponds to the city of Medellín with 400 records collected between January 2008 and December 2019. Dataset 2 corresponds to the department of Córdoba and contained 398 records collected between January 2010 and December 2021. Table 1 shows the variables included in the datasets. The first variables define SD and were selected according to WHO guidelines for the diagnosis of this type of dengue. The variables related to SD and its mortality are: extravasation, shock, bleeding and organ failure. The variables related to the treatment of this type of dengue are: blood transfusion, crystalloid solutions, colloid solutions and access to intensive care units. Finally, the decision/target variable was mortality due to SD, where 0 means that the patient recovered while 1 indicates that the patient died. The preprocessing of these datasets is described in [43].

Table 1

Brief description of the variables included in the datasets used for the experiments.

Concept	Variable type	Variable name	Description
C1	Sign	Extravasation	It is characterized by serous spills at the level of various cavities.
C2	Sign	Shock	Manifestation of severity evidenced by cold skin, thready pulse, tachycardia and hypotension.
C3	Sign	Bleeding	Blood leaks from the arteries, veins or capillaries through which it circulates, especially when it is produced in very large quantities
C4	Sign	Organ failure	Affectation of several organs due to the extravasation of liquids.
C5	Prescriptive	Blood transfusion	Routine medical procedure in which the patient receives donated blood in a vein in the arm.
C6	Prescriptive	Crystalloid solutions	Solutions containing water, electrolytes and/or sugars in different proportions.
C7	Prescriptive	Colloid solutions	Solutions with high molecular weight particles capable of increasing plasma oncotic pressure and retaining water in the intravascular space.
C8	Prescriptive	ICU	Intensive care unit
C9	Target	Mortality	Dengue mortality

4.2. Statistical validation

Eighty percent of the data was used for training and validation. During this process, the hyperparameters were tuned to select the best model with 5-fold cross-validation. The best model was evaluated on the testing set corresponding to the remaining 20% of the data. The evaluation process on the test set was repeated 100 times to perform a mean or median comparison test to determine if there were significant differences between the performances of the developed models. Before performing the comparison test between models of the same approach, the distribution of the data was determined using the Lilliefors test [44]. For this statistical test, we defined the following hypotheses:

- H_0: the data come from a normal distribution.
- H_1: the data do not come from a normal distribution.

According to the result of the Lilliefors test, we use Student's t-test because the data follows a normal distribution. The hypotheses for the comparison between two groups can be defined as follows:

- $H_0 : \bar{\mu}_{local} = \bar{\mu}_{global}$
- $H_1 : \bar{\mu}_{local} \neq \bar{\mu}_{global}$

In this way, it was possible to test the ability of the models to predict and prescribe on previously unseen data. Additionally, it was possible to test whether the difference in model performance was statistically significant. For all experiments, we defined the significance level at 0.05.

4.3. Evaluation of the models

We evaluated the models developed using classification metrics due to the categorical nature of the variables included in the datasets. In the following, we present the three metrics used with a brief description and their corresponding equation.

- *Accuracy:* percentage of correctly classified examples among the total number of classified examples.

$$Accuracy = \frac{TP + TN}{TP + FN + FP + TN} \tag{6}$$

  where TP are the true positives, TN are true negatives, FN are false negatives, and TN are true negatives.

- *Sensitivity*: it measures the ability of the classifier to predict positive cases to those actually positive.

$$Sensitivity : \frac{TP}{TP + FN} \tag{7}$$

- *Specificity*: it measures the ability of the classifier to predict negative cases to those actually negative.

$$Specificity : \frac{TN}{TN + FP} \tag{8}$$

4.4. Total federated FCM

Fig. 5 shows the architecture for this approach. In this first approach, the variables are exactly the same in all clients/sites. Here, we see that both the local models and the global model present the same variables (blue = concepts related to prediction, green = concepts related to prescription, red = target). In the following, we explain the local and global training of the models; as well as their evaluation.

4.4.1. Local training on clients

For this first case, the local training was carried out with all the variables related to the prescription to avoid mortality in patients with SD. The training was performed on each dataset of each client/site, separately. The training of the FCMs was carried out with the data-driven PSO-FCM technique, which has demonstrated its excellent performance for the optimization of matrices that generate FCMs. Subsequently, the prescriptive modeling technique PRV-FCM was used to find the optimal values of prescriptive variables. Each of these clients/sites shares the parameters, in this case, the weights matrix corresponding to the relationships between the modeled variables.

4.4.2. Global training on the federated server

After all the clients, in our case cities, train their models, the FCM construction parameters are shared to a global server, where a global model is created using the aggregation method defined in Eq. 4. One of the advantages of this approach is that the sample size of the training is increased because the patients in one client are different from those in the other clients. In this way, we increase the sample size for training. This global model is then sent to all clients, and the trained model is updated so that it can be used by each client.

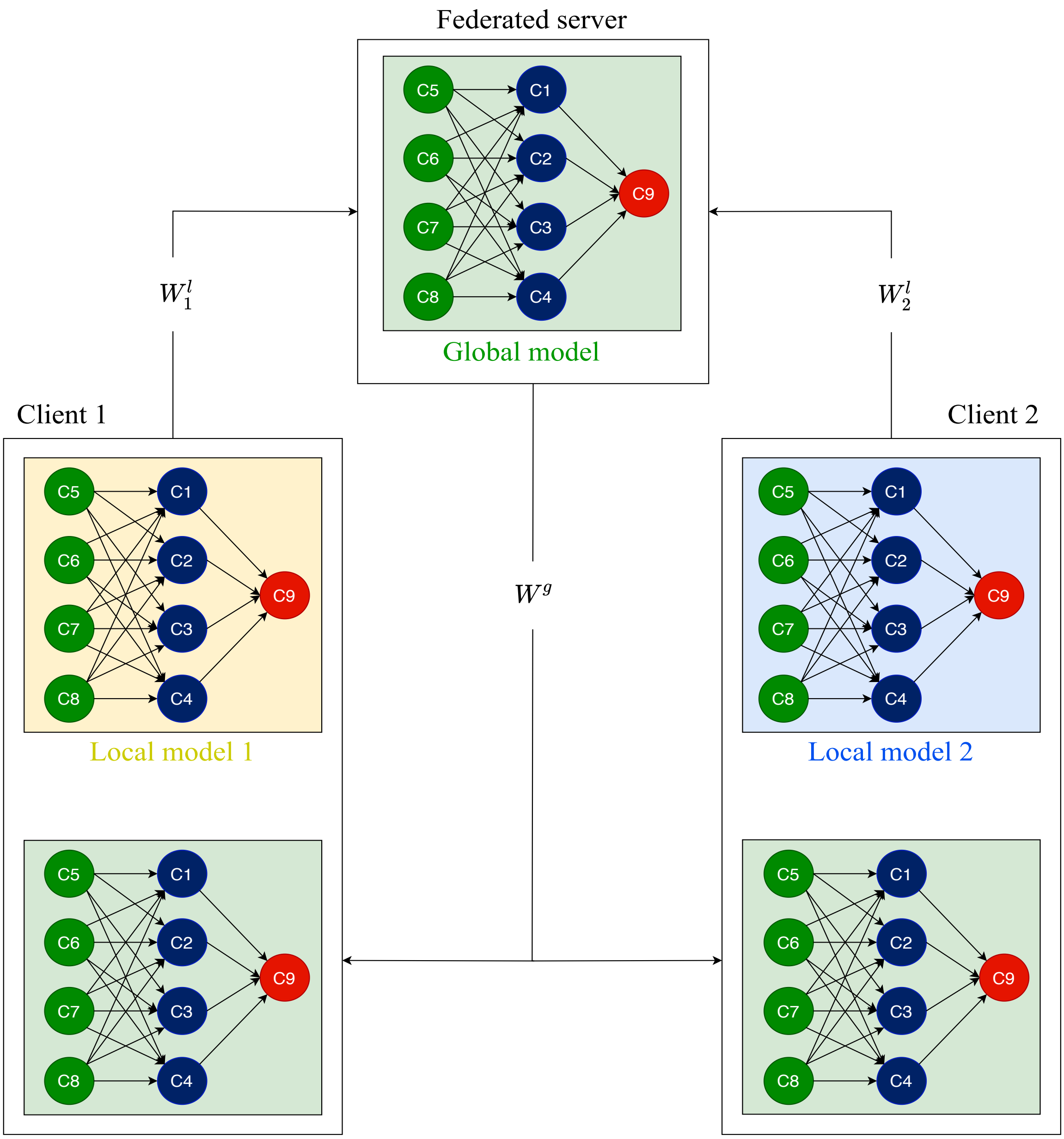

Fig. 5. Architecture of total federated FCM (the blue and green concepts are related to prediction and prescription, respectively. The red concept corresponds to the target).

4.5. Federated FCM based on the target

Fig. 6 shows the architecture for this approach. In this approach, only the target (this variable is represented in red color in Fig. 6) is common across all client data. In the following, we briefly explain the configuration of local and global training.

4.5.1. Local training on clients

In this case, the common variable is the prediction class or target. To simulate this case, we eliminate variables in the Medellin and Cordoba dataset. In each client/site, we leave two different variables so that only the target is repeated. In this way, a different predictive model of SD mortality is created for each client. The training is developed using the PSO algorithm to find the optimal weight matrix to build the FCM.

4.5.2. Global training on the federated server

The aggregation process on the federated server is a little different from the first approach. In this case, we do not use averaging to aggregate the models because the relationships between the concepts and the target are not repeated. Therefore, it is only sufficient to aggregate the two matrices into one, adding the weights of each of the clients. This process is done using Eq. 5 to create the global model. At the end, a global model is obtained that represents the information of all clients/sites. This model is updated for each of the clients so that it can be used to predict mortality from SD.

4.6. Federated FCM with transfer learning

Fig. 7 shows the architecture of the federated FCM with transfer learning. In the latter approach, learning will be transferred from one client to another because the target is located at a single client/site (see Fig. 4). For this approach, we used parameter-based transfer learning because the sample size in the two clients was approximately similar. In addition, the sign/symptom-related variables were common across the participating clients in the federation. We were interested in transfer learning because of the possibility of learning in one domain and making predictions or prescriptions in a different but related test domain. In healthcare, it is common to find healthcare institutions with treatment-related data and other institutions that collect only diagnosis-related

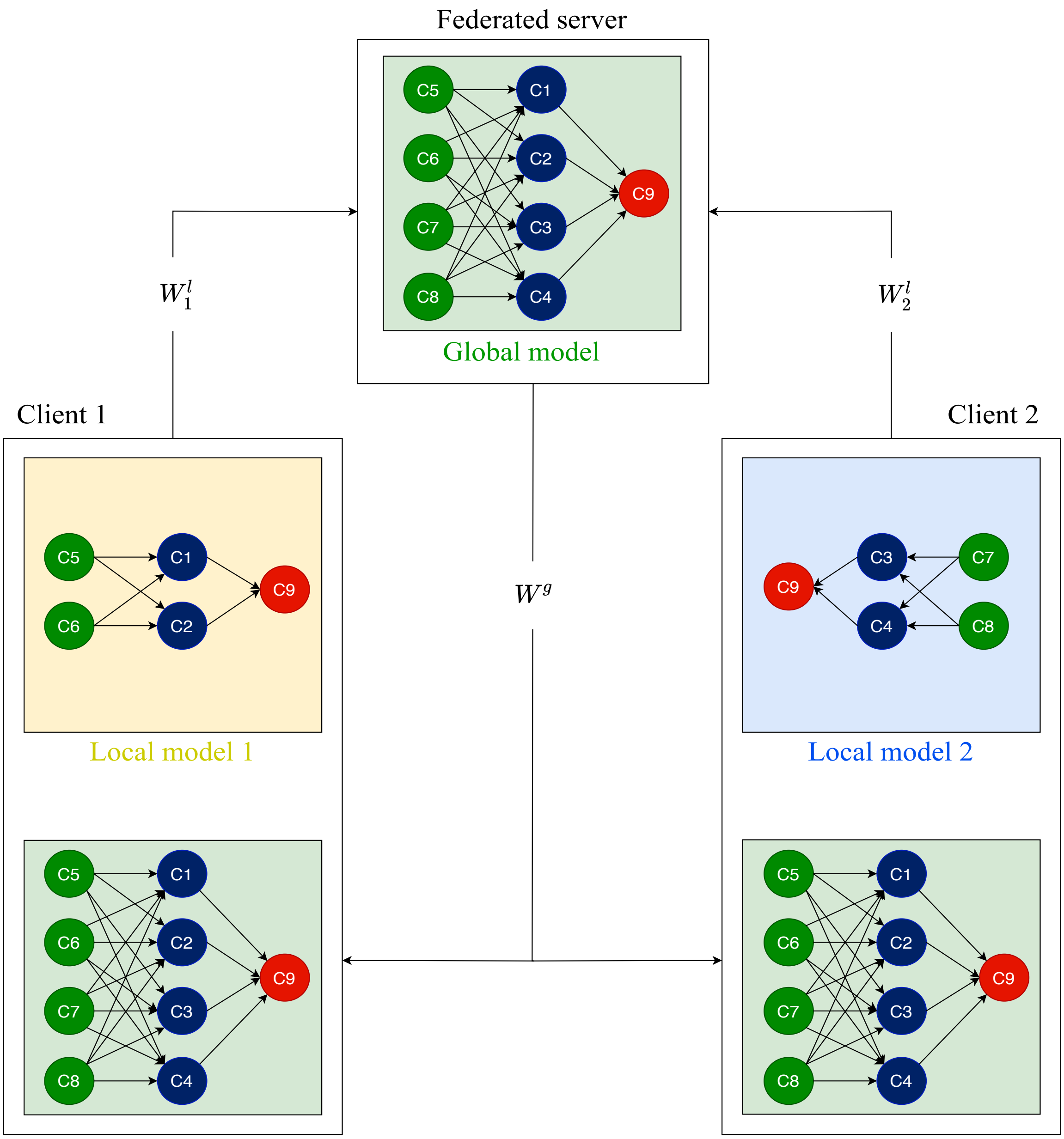

Fig. 6. Architecture of target-based federated FCM (the blue and green concepts are related to prediction and prescription, respectively. The red concept corresponds to the target).

data. Specifically, training local models with data that represent the therapeutic process of dengue, and that the extracted knowledge can be transferred to other settings, which would be of great utility to support clinical decision-making. To achieve this goal, two processes were performed: i) a local training of the prescription model (see local model 1 in Fig. 7) and its subsequent evaluation; ii) the second step consisted of a retraining of the predictive model (see local model 2 in Fig. 7) leaving constant the parameter values of the initial prescriptive model. Next, we explain the training of the variables at the local level and their update in the global model.

4.6.1. Local training on clients

The local training of each client will be different due to the presence of different variables. For example, client 1 has the prescriptive variables acting on the diagnostic variables, while client 2 has only the diagnostic variables with the target variable. For the first case (client 1), the PRV-FCM algorithm was used to build the prescriptive models (local model 1), while for the second step (client 2) the data-driven PSO-FCM algorithm was used to train the predictive model and generate local model 2.

4.6.2. Global training on the federated server

The creation of the global model was performed using the aggregation process defined in Eq. 5. This process is responsible for integrating the prediction and prescription FCMs to generate a federated global model.

5. Results and discussion

In this article, we aimed to develop and implement three federated learning approaches for FCMs to support clinical decision-making in dengue, specifically SD. In this section, we show the results obtained from the implementation of each of the proposed approaches on the described datasets. Then, we will discuss each of the results obtained in each approach. Finally, we compare our work with previous studies.

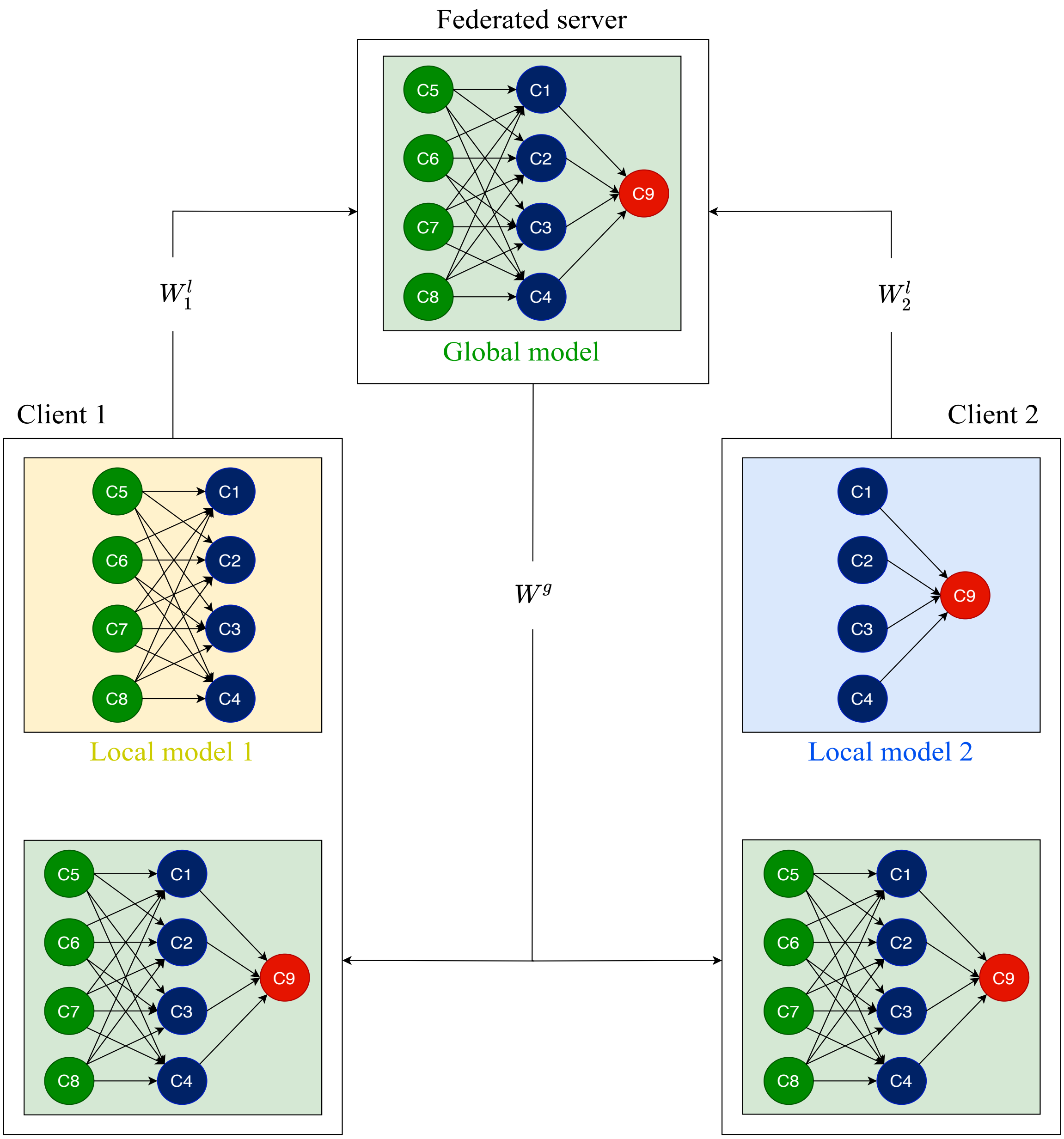

Fig. 7. Architecture of transfer learning federated FCM (the blue and green concepts are related to prediction and prescription, respectively. The red concept corresponds to the target).

Table 2

Performance of the models developed with the total federated FCM approach. * indicates the average for all prescriptive variables. NA = not applicable.

Data type	Model	Data configuration	Task	Accuracy	Sensitivity	Specificity
Signs, treatment options and target	Local 1	Local data from Medellín	Prediction	0.68	0.68	0.50
			Prescription	0.87*	0.75*	1.00*
	Local 2	Local data 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	Centralized data	Prescription	0.88*	0.83*	0.94*

5.1. Total federated FCM

Table 2 shows the results of the local models and the global models applied to the previously described datasets. Fig. 8 shows the result of 100 simulations performed during the evaluation process of the models with a total federated learning approach. Additionally, it shows the statistical comparison of the performance of the predictive and prescriptive models. Both Local 1 and Local 2 models obtained good results for prescription with accuracy values of 0.87 and 0.86, respectively. However, it can be seen that the global federated predictive and prescriptive models were superior to all the local models, including the model with centralized data. Regarding sensitivity and specificity, the results showed the same trend of accuracy where federated global models performed better than local and centralized models.

Total federated learning consisted of a federated learning approach where all client variables are common. In this way, local models can be trained with different data and the sample size can be increased to improve prediction or prescription performance. The results of the local predictive models showed the ability to predict SD mortality. The results were acceptable, with accuracies between 0.68 and 0.74. Federated learning improved these results with 0.76. This demonstrates the ability to increase the sample size with federated learning. The same was true for the prescriptive models. The federated global model performed better than local models perhaps because the sample size was larger.

Although this accuracy is good, we only used a few variables for SD. The use of only 4 system variables and 4 prescriptive variables is too few to develop more robust models. Additionally, the

Table 3

Performance of the models developed with the target-based approach. * indicates the average for all prescriptive variables. NA = not applicable.

Model	Data configuration	Data type	Task	Accuracy	Sensitivity	Specificity
Local 1	Local data 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 data 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 data centralized	All signs, treatment options and target	Prescription	0.88*	0.83*	0.94*

sample size is small, which is a limitation of the models to generalize. It is necessary to increase the sample size by adding other cities in Colombia and integrating new variables to explain their influence on mortality from SD.

5.2. Target-based federated FCM

Table 3 shows the accuracy, sensitivity and specificity of the models based on target-based federated FCM. Fig. 9 shows the result of 100 simulations performed during the evaluation process of the models with a total federated learning approach. Additionally, it shows the statistical comparison of the performance of the predictive and prescriptive models. In this approach, the target is the only variable in common between the clients. As in the first approach, the results showed that the federated global model performs better than the local models and the centralized model. One of the methodological novelties of the present work is the federated FCM approach based on the target variable. On many occasions, we have data in different locations and their only common feature is the target. This approach allows building global models where features are not repeated between datasets in different locations.

The results show the ability of our approach to predict in local environments with few variables. Local models 1 and 2 use two prescriptive variables and two diagnostic variables. Despite the small number of variables, the performance of the models is satisfactory. Additionally, the federated global model has the ability to predict and prescribe better than a model with centralized data. The sensitivity and specificity of the federated global models developed in this approach had higher performance, however, the predictive models are better able to classify positive cases than negative

Table 4

Performance of the models developed with the transfer learning federated approach. * indicates the average for all prescriptive variables. NA = not applicable.

Model	Data configuration	Data type	Task	Accuracy	Sensitivity	Specificity
Local 1	Local data from Medellín	Signs and treatment options	Prescription	0.95*	0.94*	0.93*
Local 2	Local data 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 data centralized	Signs, treatment options and target	Prescription	0.88*	0.83*	0.94*

cases (see Table 3). It is clear that the performance could be improved, either by increasing the size of the data used or by adding variables that explain the influence on dengue severity and mortality. The results of applying this approach to the data demonstrated that the use of clinical and treatment data are useful for predicting mortality and prescribing treatment to prevent death. The presence of warning signs established by the WHO has been shown to influence the severity and can be used as predictors of mortality from SD. Adding these types of variables to the models could improve their performance to obtain more robust models.

5.3. Federated FCM with transfer learning

Table 4 shows the accuracy, sensitivity and specificity of the models based on target-based federated FCM. Fig. 10 shows the result of 100 simulations performed during the evaluation process of the models with a total federated learning approach. Additionally, it shows the statistical comparison of the performance of the predictive and prescriptive models. In this latter learning approach, we can observe the ability of the federated global model to predict and prescribe with excellent performance outperforming the local models and the non-federated centralized model. In this case, as in the two previous approaches, the accuracy, sensitivity and specificity of the models were superior in the federated global model. The implementation of federated learning to transfer learning from prescription to prediction allows the integration of diagnosis and treatment of SD.

The federated FCM approach with transfer learning is an approach, which can be used to transfer learning from one domain to another. In our case, we were able to transfer learning from SD treatment to the mortality prediction domain.

Of the three approaches, this was the one that gave the best results for the prescription. It is true that the division of the data in this approach allowed separating the domains, and only left the important variables in each part of the architecture. In the client with prescriptive variables and clinical manifestations, the relationship between treatment and the defining signs of SD is evident. Predicting SD mortality with only the defining variables remains a challenge. Using only four variables to predict mortality from this type of dengue is not enough to have models with excellent performance.

Finally, the statistical tests performed, whose significance values (p-values) are inserted in Fig. 8, Fig. 9 and Fig. 10 for the three approaches show that there are significant differences between the models developed.

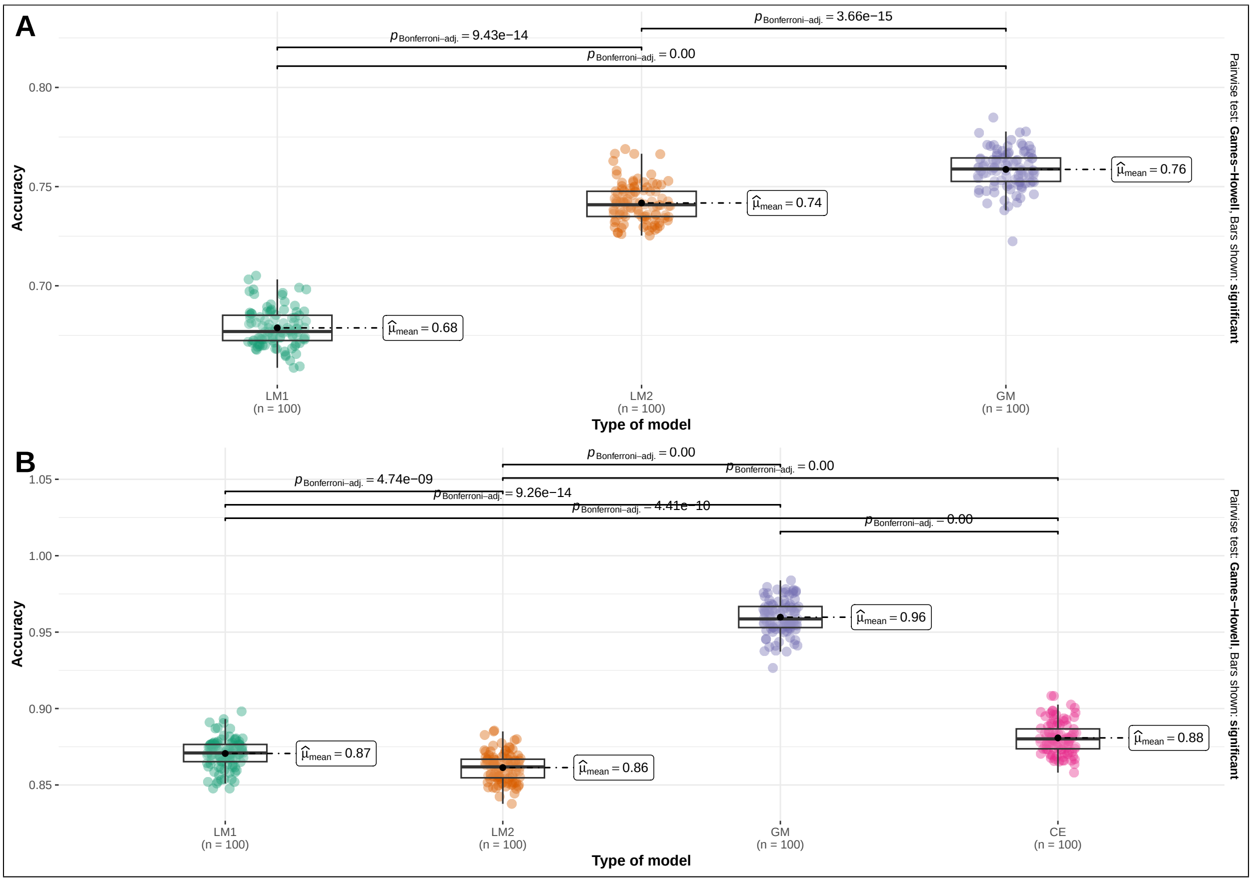

Fig. 8. Boxplots to compare the models' performance in a total federated learning approach. A and B correspond to the predictive and prescriptive models, respectively. Abbreviations: LM1 = local model 1, LM2 = Local model 2, GM = global model, CE = centralized approach.

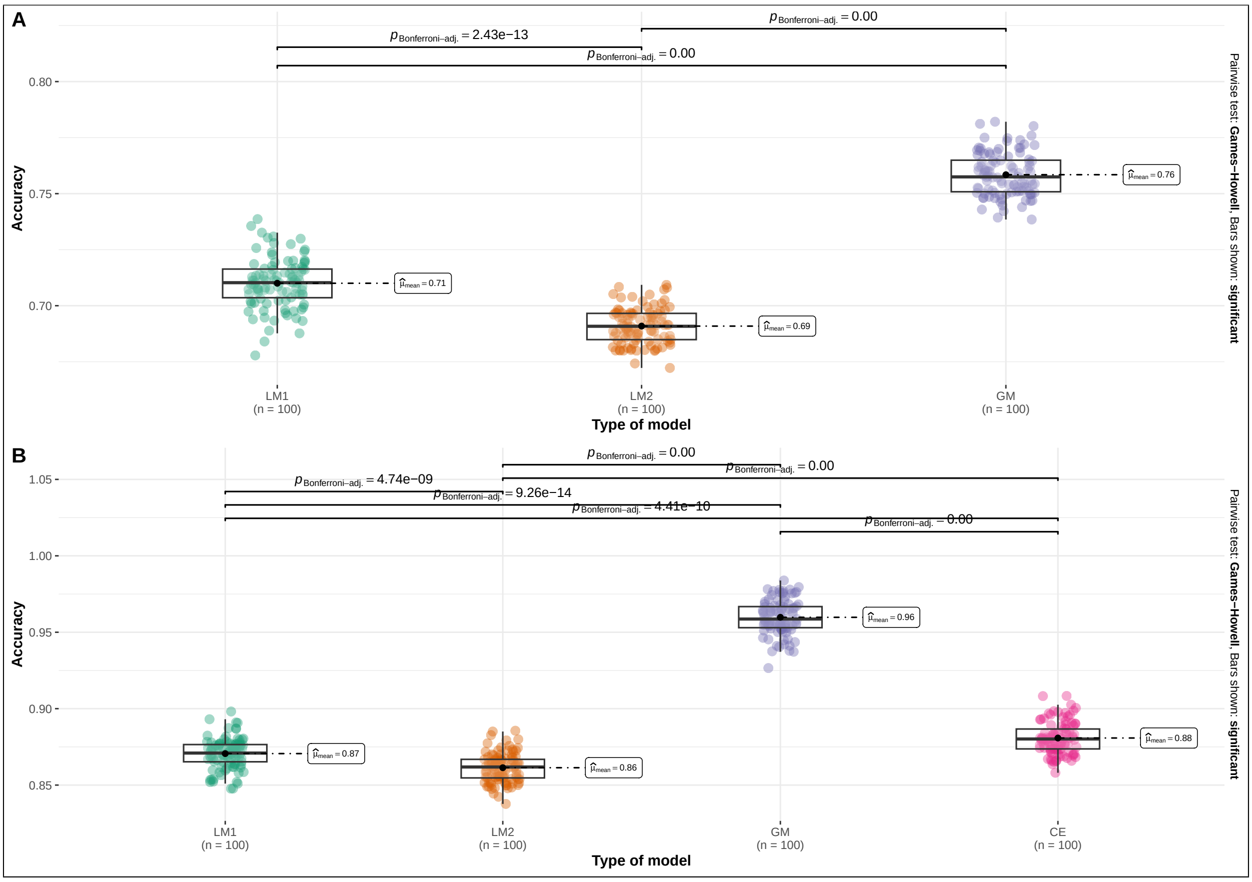

Fig. 9. Boxplots to compare the models' performance in a target-based federated learning approach. A and B correspond to the predictive and prescriptive models, respectively. Abbreviations: LM1 = local model 1, LM2 = Local model 2, GM = global model, CE = centralized approach.

5.4. Comparison with previous work

In this section, we compared the results of the present work with previously developed approaches published in the literature. Initially, we performed a qualitative comparison with other federated learning approaches that have been implemented in medical settings. On the other hand, since this is the first paper to propose federated learning approaches for FCMs for the clinical management of SD, we compared our results with prediction and prescription models for the clinical management of SD with centralized approaches.

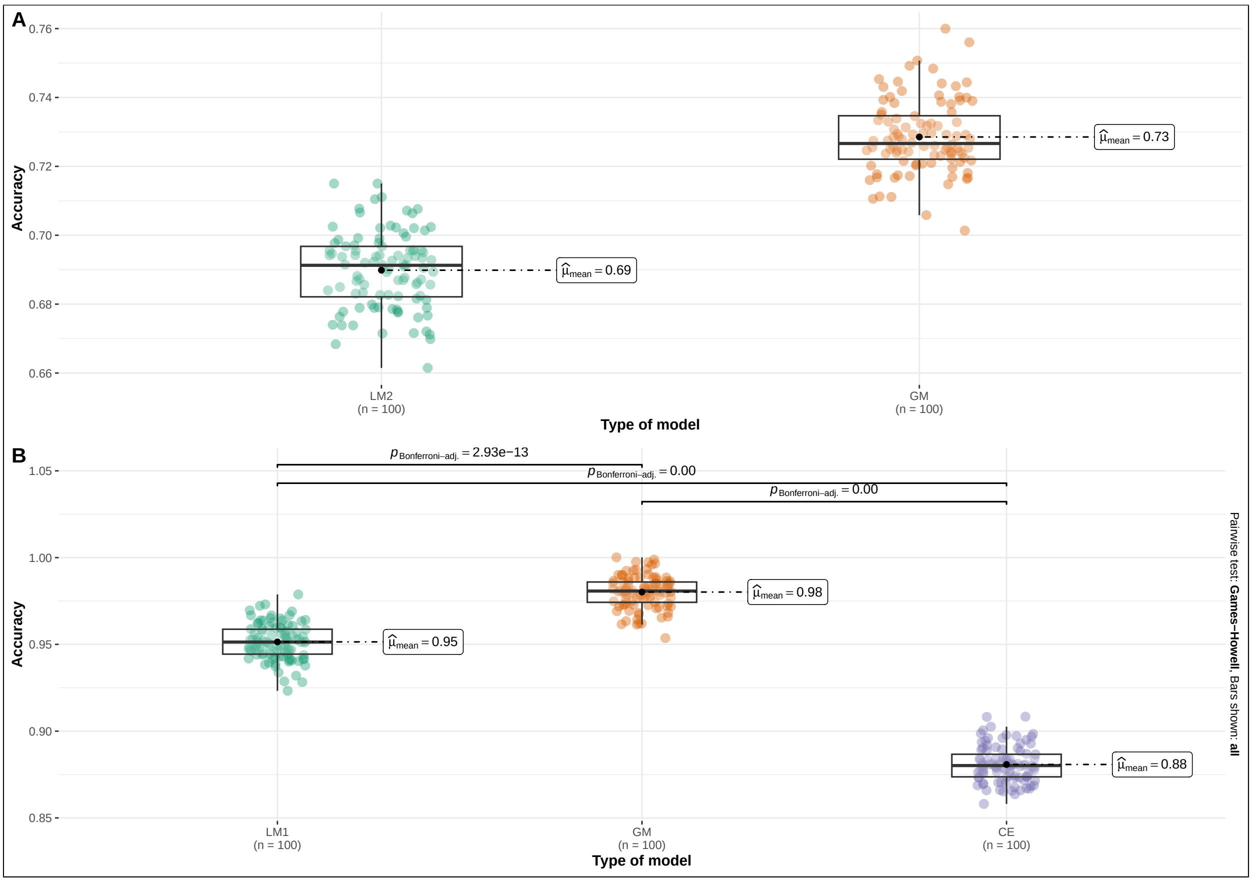

Fig. 10. Boxplots to compare the models' performance in federated transfer learning. A and B correspond to prescriptive and predictive models, respectively. Abbreviations: LM1 = local model 1, LM2 = Local model 2, GM = global model, CE = centralized approach.

5.5. Qualitative comparison

We performed a qualitative comparison of our work with other studies due to the lack of research implementing federated learning for SD. We used qualitative criteria defined in Table 5 for comparison with other approaches reported in the literature. The first criterion is related to the use and implementation of artificial intelligence techniques for the generation of predictive models for diagnosis. The second criterion evaluates the use and implementation of prescriptive models for disease treatment. The third criterion evaluates the ability of proposed systems to have an integration of predictive and prescriptive models in the federated learning environment. Finally, the last criterion indicates the ability of the approach to be intuitive and easily adaptable.

Table 5

Qualitative comparison between previous studies and our work.

Qualitative criteria	Work				
	[36]	[45]	[46]	[47]	Our work
AI models with FL for diagnosis	✓	✓	✗	✓	✓
AI models with FL for treatment	✗	✗	✓	✗	✓
Integration of AI models with FL for diagnosis and treatment	✗	✗	✗	✗	✓
Ease of use and adaptability	✓	✓	✓	✓	✓

Federated learning has been widely implemented in different fields of medical application [36, 45–47]. For example, Salmeron and Arevalo [36] developed a federated learning approach using computational intelligence techniques such as PSO and FCM for cancer diagnosis. The authors implemented an identical structure of FCMs across all clients or federation participants and demonstrated the ability of the federated approach to generate models with higher performance than local models. However, this work does not integrate prescriptive models with federated learning, nor does it integrate disease diagnosis and treatment. The proposed system is intuitive and easily adaptable. Another work developed by Li et al [45] supports decision-making in colorectal cancer prognosis by using random forests to build multi-center predictive models. The approach proposed by Li et al is easy to use, adaptable to any medical institution and is aimed at supporting decision-making with respect to diagnosis, guarantees the privacy of patient data, but does not generated treatment-oriented actions. Liu and Yang [46] trained a robot with deep learning to support physicians with the treatment of patients with depression. The work developed by Liu and Yang is novel and ensures privacy of patient data with federated learning. However, this approach only focuses on treatment and does not support decision-making for a depression diagnosis. Finally, a work developed by Li et al [47] preserved data privacy using a federated learning approach for Alzheimer's disease detection. The developed system used classification models and performed well in diagnosing the disease. Moreover, it can be adapted for the aggregation of new features to increase prediction performance.

In contrast to the previously presented work, we implemented three federated learning approaches with different architectures for predictive and prescriptive model generation. These approaches use different configurations to support decision-making in the diagnosis and treatment of SD using AI techniques. The integration of predictive and prescriptive models for diagnosis and treatment could be more useful than generating models only for diagnosis or only for treatment. The systems generated in each of our proposed approaches are also intuitive and their easy adaptation would allow the addition of other important variables for the analysis of SD.

5.6. Quantitative comparison

Although the availability of data regarding SD mortality remains scarce, which has led to the development of models based on the expertise of experts [14], our models performed well for both predicting and prescribing when compared to previous work based on data reported in the literature. For example, Hoyos et al [43] developed prediction models for SD mortality using the same dataset used in the present study. The authors developed the models with FCMs with average accuracies of 0.74. Another similar work is developed by Chattopadhyay et al. [48] where they developed classification models to predict dengue death with a maximum performance of 0.72 of accuracy in a smaller sample size (100 patients). Regarding prescriptive models, the PRV-FCM methodology yielded excellent results due to its ability to find optimal values using the FCM inference process and optimization algorithms. Our results confirm the results reported by several previous studies where the prescriptive capability of PRV-FCM in medical settings has been demonstrated.

6. Conclusions

We set out to develop three federated learning approaches for FCMs to support clinical decision-making in dengue, specifically SD. Each approach consisted of clients/sites with different/equal data depending on their settings. For each approach, predictive and prescriptive models were built using FCMs and optimization algorithms. The results showed that the three federated learning approaches with FCMs outperform local models trained on private data. Additionally, the federated approach outperforms models trained with centralized data. Finally, it is shown that federated learning approaches are useful for fields of science where data security and privacy must be guaranteed.

This work has some limitations. For example, the approaches are distributed but centralized, because a single federated server does the aggregation process. If this server has problems or is unavailable due to some circumstances, then the global model cannot be updated. For this reason, it is necessary to develop decentralized federated models. For example, an aggregation process can be performed in all the nodes of the system, so that if one node stops working, the others have a backup of the information and the aggregation information is not lost.

Another limitation of the present study is the number of clients used for the simulations. In this case, we only used two clients due to data availability. It is recommended to apply these approaches on larger clients to analyze the predictive and prescriptive capabilities of both local and global models. Finally, the approaches were not validated in licensed clinical institutions. Strict validation of these approaches in hospitals or clinics in Colombia would be useful to understand its usefulness in decision-making in clinical settings.

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Conflict of interest

The authors declare no conflict of interest.

CRediT authorship contribution statement

William Hoyos: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Validation, Visualization & Writing – original draft. **Jose Aguilar:** Conceptualization, Formal analysis, Resources, Supervision, Writing – reviewing & editing. **Mauricio Toro:** Resources, Supervision, Writing – reviewing & editing.

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