FortiRx 2.0: Smart Privacy-Preserved Demand Forecasting of Prescription Drugs in Healthcare-CPS

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***Abstract*—Pharmaceutical Supply Chains (PSCs) are a combination of processes and networks involved in the production, distribution, and delivery of pharmaceutical products from the stage of raw materials till they reach the end-user which is typically patients. PSC is a complex and critical part of the Healthcare Cyber-Physical System (H-CPS) that ensures the availability, quality, and timely delivery of pharmaceutical products to meet the needs of the patients. One of the main characteristics of efficient PSC is accurate production planning and resource allocation which not only reduces the costs but also significantly enhances customer satisfaction. Accurate production planning for manufacturers needs accurate demand prediction models in place, otherwise can lead to overstocking or under-stocking, wastage, and other costs. Demand prediction of pharmaceutical products is very complicated due to unexpected fluctuations due to seasonality, pandemics, and several other reasons. This causes supply chain disruptions which may in turn cause both life and financial losses. Many statistical methods and machine learning models including time series analysis for forecasting the demand based on historical, but the significant setback is the availability of real-time data and privacy concerns on prescription data being shared. The current proposed FortiRx 2.0 architecture leverages a blockchain-based prescription system and federated learning approach to solve these issues and provide accurate demand forecasting. Federated XGBoost is used for demand prediction and different evaluation metrics are computed for performance evaluation of implemented model. These metrics are compared with baseline models Naive and Seasonal Naive as a reference and the results from the comparison are discussed.**

***Keywords*—** Healthcare Cyber-Physical System (H-CPS), Pharmaceutical Supply Chain, Prescription System, Blockchain, Distributed Ledger Technology, Federated Learning, Demand Forecasting, Time-Series Analysis, XGBoost

I. Introduction

The pharmaceutical Supply Chain (PSC) is a critical component of the Healthcare Cyber-Physical System (H-CPS) which helps connect all the processes and entities together to facilitate the planning, production, distribution, and delivery of pharmaceutical products to the consumer [1]. Typical PSC consists of multiple entities that interact in complex ways creating an entangled system. Some of the important entities in PSC are Raw material suppliers, who are responsible for supplying both Active Pharmaceutical Ingredients (API) and required Excipients to the manufacturer. The manufacturer is responsible for planning and producing pharmaceutical products in large quantities called lots. The wholesaler/ Distributor is responsible for purchasing these lots from the manufacturer at Wholesale Acquisition Cost (WAC) and sending them to the further parts of the supply chain. Retailers, Healthcare units, and pharmacies act as accessible locations for patients through which prescribed medicines are disbursed. Several other entities like Insurance companies and Pharmacy Benefit Managers (PBMs) also exist that take care of the insurance mechanisms [2]. Due to significant lead times involved in acquiring the raw materials, manufacturing process, and distribution large inventory is maintained at all the entities to facilitate the smooth operation of the supply chain and meet customer needs. Enterprise Resource Planning (ERP) systems help in managing such stock management, but still due to unpredictable demand, disease outbreaks, changes in healthcare policies, sudden shifts in patient needs, and several other factors can disrupt the PSC and cause overstocking and understocking issues. These disruptions not only cause monetary loss but also can lead to significant life loss.

Fig. 1. Problems with Demand Forecasting Models (DFMs) in Pharmaceutical Supply Chain (PSC.)

Even a small change in the demand at the consumer level can progressively increase the fluctuations in the upstream of the supply chain. This phenomenon is coined as the Bullwhip effect [3]. This type of fluctuation can cause significant inventory management issues and reduce supply chain efficiency. Patient needs are ever-changing and a small variation in prescription orders due to serious illness, public health crises, and patient behavior changes can lead to large fluctuations in orders placed by the distributor, wholesaler, and manufacturers. One of the most significant sources for these fluctuations is the Demand Forecast Models (DFMs) used for inventory predictions. Many DFMs based on different statistical and Artificial Intelligence (AI) techniques are being used in PSC for accurate demand predictions which can be used for efficient planning of production and distribution. Most of these methods use time series analysis on historical sales data to find seasonal variations and capture consumer behavior. These forecasting methods used still don't provide accurate predictions due to the unavailability of real-time sale data and other issues as shown in Figure 1. Considering these DFM errors, entities participating often carry an inventory buffer called safety stock. Employing such safety mechanisms still does not make the supply chains robust as we can see the recent pandemic COVID-19 has disrupted the supply chain operations significantly [4]. Hence, there is a dire need to develop robust DFM to avoid such disruptions in the supply chain and meet customer demands. Retail pharmacies and healthcare units make use of Point-of-Sale (PoS) systems which provide invaluable data about usage patterns, patient behavior, and healthcare provider preferences that can help in creating accurate DFMs. Prescription data with demographic information can also help in the segmentation of the market and capture demand variations based on patient groups. The frequency of filling the drugs can also help in analyzing the disease conditions in a region along with providing insights into seasonal trends.

Proposed FortiRx 2.0 makes use of the blockchain-based e-prescription system FortiRx proposed in [5] which can provide real-time and secure prescription sharing from healthcare units to the pharmacies. Considering the privacy of the patients, a robust Cipher Text-Policy based Attribute encryption is used in the proposed architecture of FortiRx. E-prescriptions are part of Electronic Health Records (EHRs) which cannot be shared with any other entities without the consent of the patient. To avoid data sharing and protect the privacy of the patients, a federated learning approach is proposed in FortiRx 2.0 which doesn't transport the patient prescription information to other entities like distributors, wholesalers, or manufacturers.

The rest of the paper is organized as follows: Section II discusses novel contributions of the proposed FortiRx 2.0. Section III gives an overview of prior related research. Section IV describes the architecture of proposed FortiRx 2.0 followed by Section V giving experimental validation and implementation details. Section VI provides results and analysis, and Section VII provides conclusions along with future scope.

II. Novel Contributions

Below are the problems with DFMs in the pharmaceutical industry which are addressed in the proposed FortiRx 2.0 along with novel solutions proposed.

A. Problems with Creating Accurate Demand Forecast Model in Pharmaceutical Industry

Some of the problems in creating an accurate DFM that are addressed by the novel proposed FortiRx 2.0 architecture are:

- Overstocking and understocking issues is the most common problem in PSC due to inaccuracies of prediction models used.
- Supply chain disruptions are very common due to the non-availability of real-time sales data.
- Prescription information is part of EHR which needs to be privacy preserved and cannot be shared among other entities without patient consent.
- Some of the third-world countries still rely on paper-based prescription systems.
- Data captured for training the models have outliers which can significantly impact the prediction which can in turn create a Bullwhip effect in the supply chain.

B. Novel Solutions Proposed

Novel contributions proposed in FortiRx 2.0 are:

- Utilizing real-time prescription information can help in creating accurate DFM that reduces overstocking and understocking issues in the supply chain.
- Blockchain leveraged decentralized architecture can help in real-time sales data available.
- Federated learning approach and CP-ABE access control mechanism ensures the privacy of the patients and doesn't reveal the patient prescription information to unintended parties.
- Blockchain-based approach helps in creating a cost-effective and adaptable E-Prescription system.
- The Trust model through consensus protocols ensures no outliers and helps in the accuracy of the DFM.

III. Related Prior Research

Globalization has made the distributed entities that are physically apart work collectively and share the resources to make products available in every corner of the world. This has created a complex supply chain environment that will have many interactions for the product to move from manufacturing till it reaches the consumer. PSC is one such complex environment that facilitated the availability of prescription drugs at the right place in the right quantities to the right patient through the right path. Seasonality and ever-changing demand for prescription drugs made the DFM and production planning difficult in PSC and caused supply chain disruptions. Recent technological advancements like blockchain and AI technologies can help in solving this issue and avoid such disruptions. Blockchain technology which started as a financial solution has shown promising solutions for making robust pharmaceutical supply chains [6], [7], [8] and E-Prescription systems [9], [10]. Architecture proposed in [9] uses Ethereum blockchain technology for management and validation of ePrescription and also some security measures were implemented for restricted access. However, current solution address data sharing between dynamic group of users by Cipher Text Policy Based Encryption (CP-ABE) and also provides accurate DFM for prescription drugs. Architecture proposed in [10] also focuses on patient-centric architecture for managing prescription while using multi-signature confirmations. However, proposed FortiRx 2.0 can efficiently manage large amounts of information utilizing off-chain data storage while also preserving the privacy by leveraging CP-ABE based security model.

Methods proposed in [11] have evaluated multiple machine learning and deep learning models including Seasonal Autoregressive Integrated Moving Average (SARIMA), Prophet from Facebook, linear regression, Random forest, XGBoost, and Long Short-Term Memory (LSTM) for analyzing the inventory sale histories and determined the SARIMA model outperforms others in accuracy of prediction with minimal Mean Absolute Error (MAE). Another study [12] has explored irregularities in medicine demand forecasting using Croston's method, Syntetos-Boylan Approximation (SBA), Teunter Syntetos and Babai's (TSB) methods and compared the efficiencies with methods proposed in [13]. A case study on Barij pharmaceutical company demand prediction using a fuzzy interface system combined with cellular automata is proposed in [14]. This method utilized the sale data from 84 drugstores in a region of Tehran and determined the demand at each drugstore.

XGBoost is an efficient machine algorithm to perform both classification and regression tasks. It is most widely used for time series analysis compared to ARIMA and VAR models because of its performance and predictive power. Apart from pharmaceutical product demand, XGBoost with and without Fourier eigenvalues is used for demand prediction of passenger-carrying taxi hot spot areas [15]. Another implementation of XGBoost for taxi demand prediction is done in [16].

The use of prescription information for demand prediction of pharmaceutical products is not much explored and such a solution is very much needed for efficient management of the PSC. In our current proposed novel FortiRx 2.0, XGBoost is used for implementing a DFM, and the quality of data is maintained by leveraging blockchain. Privacy of the patient information is also preserved by utilizing a federated learning approach which increases efficiency while providing data privacy.

IV. Architectural Overview of FortiRx 2.0

An architectural overview of the proposed FortiRx 2.0 is shown in Fig. 2. FortiRx 2.0 is the extension of the proposed FortiRx in [5] which is a blockchain-based prescription system. This system utilizes smart contracts to implement the business logic which includes the issuance, update, requesting, and issuing of refills of prescription drugs while providing a reliable way of authenticating prescription information. It also implements a Role-based Access Control Mechanism (RBAC) combined with Cipher-Text Policy Encryption (CP-ABE) to preserve patient privacy. FortiRx also takes care of scalability by storing the encrypted prescription information off-chain distributed data storage, reducing the cost and time to process a transaction in the system. CP-ABE encryption uses an access tree structure consisting of the attributes in the form of a tree structure assigned by the trusted authority. Participants with assigned attributes satisfying the defined tree structure are only able to decrypt the prescription information. These attributes can include, name, location, specific employee id, time, etc. This prescription information at each pharmacy location is used in FortiRx 2.0 as the real-time local dataset. Each pharmacy acts as the federated client for generating the updates for local model in real time.

Federated XGBoost is used in the proposed FortiRx 2.0 architecture which uses the previous sales data aggregated from the Point-of-Sale (PoS) data. Federated XGBoost is an advanced machine learning technique that combines XGBoost a gradient-boosting algorithm with principles of federated learning. This allows for performing model training collaboratively across multiple distributed devices instead of the most used centralized model training. As the client data is not moved from clients to the centralized servers for model training, the privacy of client data is protected. This kind of approach is valuable while handling sensitive client information from distributed data sources. Along with distributed data sources, this approach can also handle data heterogeneity. As there is no need for entire client data to be moved to the centralized servers, the data communication overhead is also addressed in a federated approach. Different steps involved in federated XGBoost are discussed in the current Section.

Data Partitioning

Data is partitioned into local datasets and resides at each local pharmacy. Each of these federated clients preserves the privacy of the local data and doesn't share them with the centralized server. The data at each client is non-overlapping and represents its local dataset. Let C represents the set of clients participating in collaborative training $C = \{c_1, c_2, \ldots, c_n\}$. Local dataset at each client c_i is represented by D_{c_i} and calculated using the following expression:

$$Dataset\ \mathcal{D} = \bigcup_{i=1}^{n} D_{c_i}. \tag{1}$$

Local XGBoost Model Training

Each client loads the local dataset and trains the local XGBoost model using initialized parameters. Training will be performed iteratively to improve the model through gradient boosting using hyperparameters Θ_{c_i}). Once the local model is trained, the model will be stored locally. Each client c_i trains the local model M_{c_i} using the local dataset D_{c_i} as follows:

$$M_{c_i} = \text{XGBoostTrain}(D_{c_i}, \Theta_{c_i}). \tag{2}$$

Initialization of Global Model

A starting point global model M_{global} is initialized at the server using global hyperparameters Θ_{global} as follows:

$$M_{\text{global}} = \text{XGBoostInitialize}(\Theta_{\text{global}}). \tag{3}$$

Federated Training Iterations

Number of iterations of federated training is determined by a pre-determined value T. Each iteration every client c_i generates a model update which are gradients ∇_{c_i} and/or hessians $\mathcal{H}_{c_i}$ as follows:

$$\nabla_{c_i}, \mathcal{H}_{c_i} = \text{CalculateGradientsHessians}(M_{c_i}, D_{c_i}). \tag{4}$$

These computed gradients and/or hessians will be packaged as model update Ψ_{c_i}. Packaged model updates Ψ_{c_i} are computed as follows:

$$\Psi_{c_i} = \text{PackageModelUpdate}(\nabla_{c_i}, \mathcal{H}_{c_i}). \tag{5}$$

These updates are then communicated back from the client c_i to the centralized server for aggregation of model updates as follows:

$$\Psi_{\text{aggregated}} = \text{AggregateModelUpdates}(\Psi_{c_1}, \Psi_{c_2}, \ldots, \Psi_{c_n}). \tag{6}$$

Agreegated global model is then sent back to all the clients C as follows:

$$\Psi_{\text{aggregated}} \rightarrow \{c_1, c_2, \ldots, c_n\}. \tag{7}$$

Every client c_i will update its local model by integrating the aggregated global model. Aggregated global model M_{c_i} is computed as follows:

$$M_{c_i} = \text{XGBoostIntegrate}(M_{c_i}, \Psi_{\text{aggregated}}). \tag{8}$$

Updated local model is then further trained with local dataset D_{c_i} by every client c_i. Updated local model M_{c_i} is computed as follows:

$$M_{c_i} = \text{XGBoostTrain}(D_{c_i}, M_{c_i}). \tag{9}$$

Iterations are repeated until the number of iterations T is reached and the resultant global model is used as the DFM for predicting pharmaceutical product demand.

V. Experimental Validation of Proposed FortiRx 2.0

A. Dataset and Exploratory Analysis

Pharma sales data given in [17] is used for simulation and analysis of proposed FortiRx 2.0. This dataset covers sales data collected over the period of 6 years from 2014-2019. Selected groups of drugs are then classified into 8 Anatomical Therapeutic Chemical (ATC) classification systems: M01AB, M01AE, N02BA, N02BE, N05C, N05B, R03, and R06. Feature engineering and data cleaning functions are already performed and the datasets for hourly, daily, and weekly sales are made available in [17]. Data description for each of these datasets is shown in Table I.

TABLE I
Details of datasets.

Dataset Name	Frequency	No.of Recordings
saleshourly.csv	Hourly	656928
salesdaily.csv	Daily	27390
salesweekly.csv	Weekly	2726
salesmonthly.csv	Monthly	638

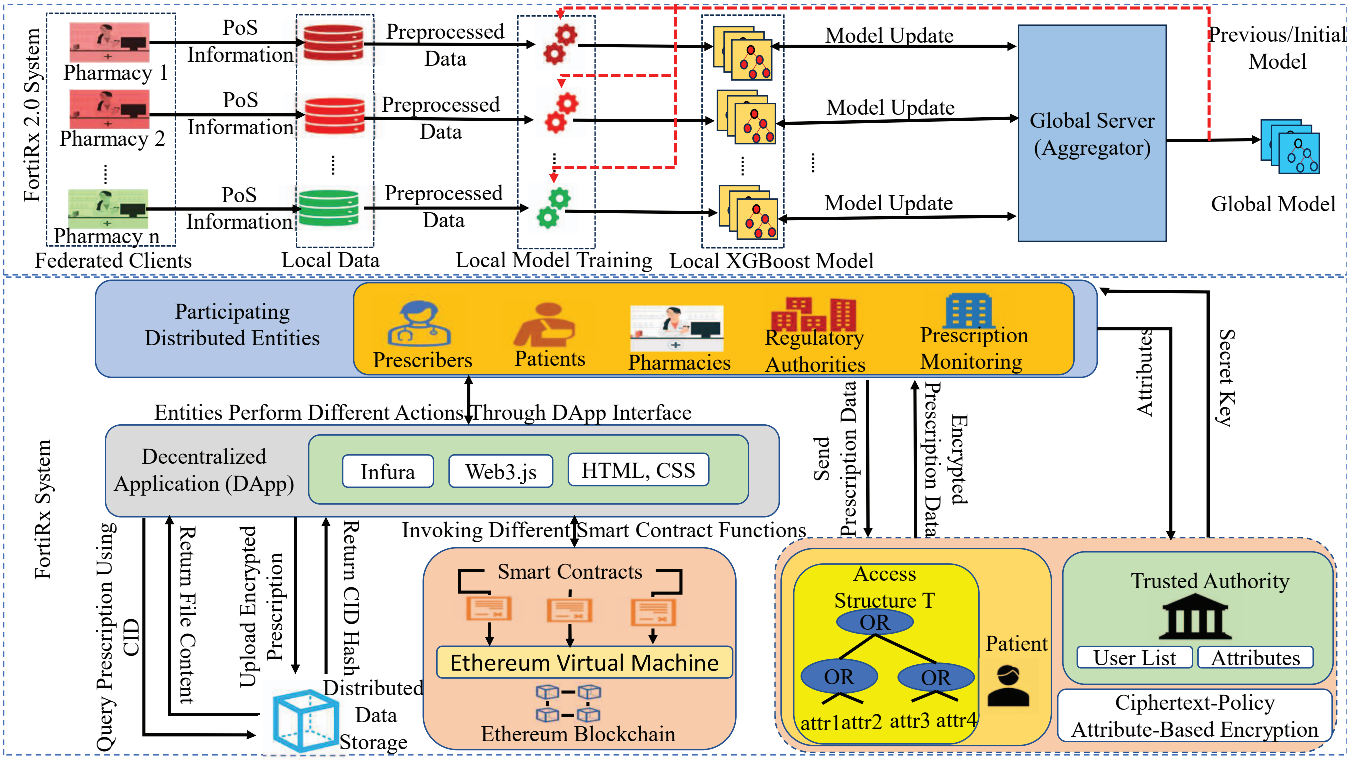

Fig. 2. Architectural Overview of Proposed FortiRx 2.0

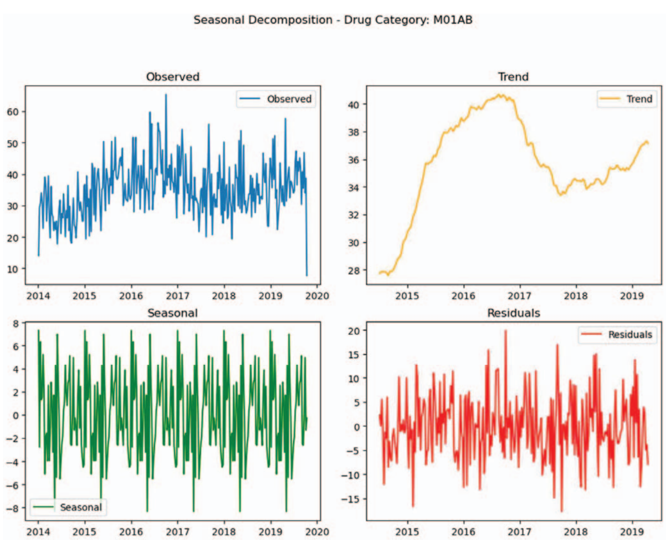

Fig. 3. Seasonal Decomposition for Drug Category M01AB

Seasonal decomposition helps in breaking down the time-series data into fundamental components like trend, seasonality, and residual which can give insights into underlying patterns and behaviors. Seasonal decomposition is performed on the weekly sales data for all 8 ATC categories. Seasonal decomposition for drug categories M01AB, N02BA and R03 are shown in Figures 3,4 and 5 respectively. As we can see, the trend of drug sales is fluctuating over time from the year 2014 to 2019 for MA01AB gradually decreasing for N02BA while it is increasing gradually for R03.

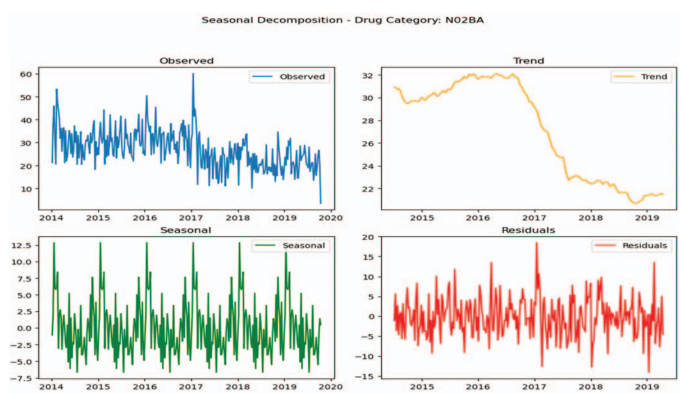

Fig. 4. Seasonal Decomposition for Drug Category N02BA

B. Implementation

We implemented our proposed FortiRx 2.0 in Python using a Windows 11 desktop with 11th gen Intel i7-11700F @ 2.50GHz, 16GB RAM, and GPU GeForce RTX 3060 12 GB. To implement federated learning Flower [18] is used. Flower is a framework designed for leveraging federated learning solutions with a wide variety of configurations as per the needs of individual use cases. The implemented prototype for evaluation consists of 5 clients and 1 server and the dataset is split into 5 non-overlapping local datasets. Before splitting, the dataset is divided into 80%-20% split for training and testing purposes. Configuration of federated learning is shown in Table II.

Once the models are trained, there are two approaches for evaluating the model. Either it can be done in a centralized (at the server) or federated evaluation (at the client side). In the current

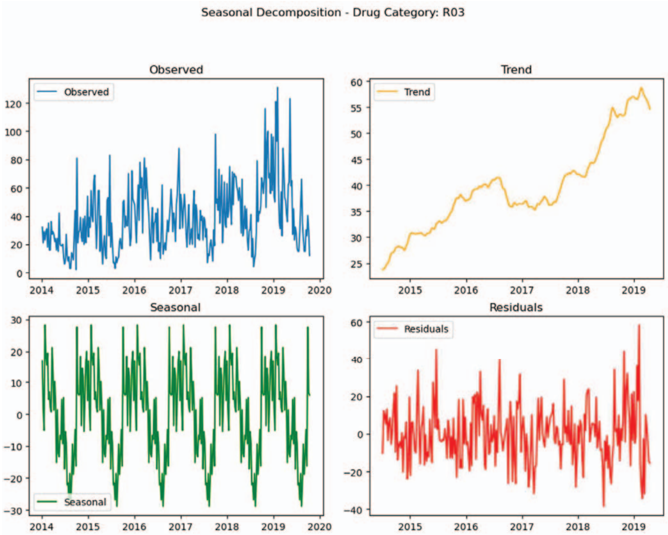

Fig. 5. Seasonal Decomposition for Drug Category R03

TABLE II
FEDERATED XGBOOST CONFIGURATION PARAMETERS

Parameter	Value
Train Split	80%
Test Split	20%
Number of Communication Rounds	15
Local Training Iterations	100
Model Update Aggregation	FedAvg
Batch Size at Client	64
Fraction of clients selected for evaluation	1.0
Minimum Number of Clients Need to be Connected	1

implementation, centralized evaluation is performed with two evaluation metrics Loss and Mean Squared Error (MSE). To compare the performance of the implemented federated learning approach, baseline forecasting performance is evaluated. Naive forecasting is one of the simplest time-series forecasting methods which is usually used for baseline performance analysis when compared with the more advanced forecasting model. The naive model assumes the future value of the time series is the same as the last observed value of the series as shown below where t is the current time step. Naive model forecast value is shown as follows:

$$Forecast_{\text{t+1}} = Actual_t. \tag{10}$$

Along with this, another baseline model used as a reference model is seasonal naive when dealing with seasonal time series data. Seasonal naive assumes the value of at next season cycle is the same as the corresponding previous season cycle as shown below where t is the current time step and k is the length of the seasonal cycle. Seasonal naive forecast values is shown as follows:

$$Forecast_{\text{t+1}} = Actual_{\text{t+1-k}}. \tag{11}$$

Implemented federated XGBoost is compared to these baseline models to determine the performance.

VI. RESULTS AND DISCUSSION

Evaluation metrics used for comparing the performance of implemented federated XGBoost with base reference models are Loss and

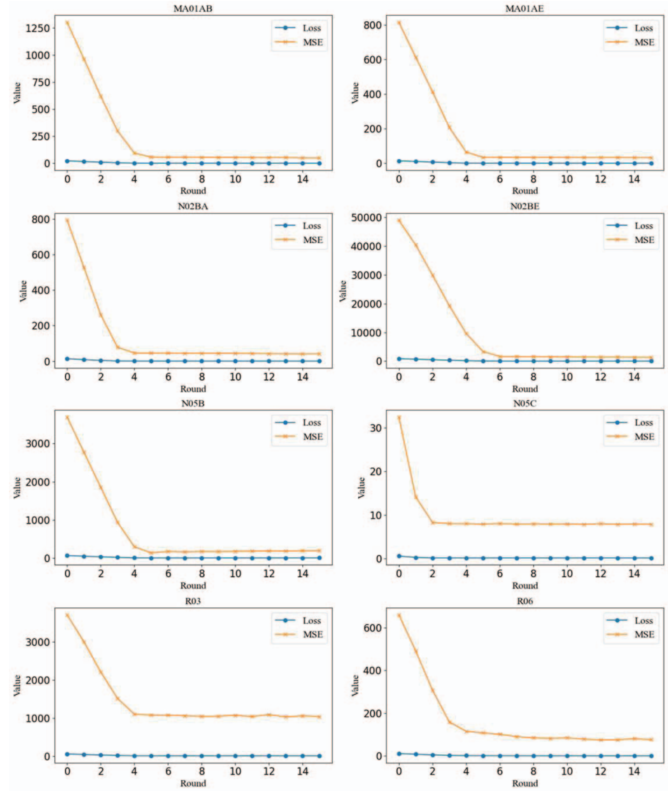

Fig. 6. Loss and MSE metrics for Each Drug Type at Each Round of Federated Learning

Mean Square Error (MSE). The loss function measures the difference between the predicted values from the actual values. Let the Loss L with predicted value $\hat{y}$ and actual value y can be computed using the following expression:

$$L_i(\hat{y}_i, y_i) = (\hat{y}_i - y_i)^2. \tag{12}$$

Mean Square Error (MSE) is another important metric that is evaluated in regression tasks. Given N data points with predicted value $\hat{y}$ and true value as y. MSE is computed as follows:

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(\hat{y}_i - y_i)^2. \tag{13}$$

Computed Loss and MSE for each drug type at each round of federated learning are plotted and shown in Figure 6. As we can see for every drug type the loss and MSE metrics are gradually reducing with each round which signifies the learning process is improving the model resulting in more accurate predictions. After a few rounds of federated learning, the learning rate saturates, and no further rounds can improve the model.

A comparison of implemented federated XGBoost with baseline metrics is shown in Table III. The MSE values of implemented federated XGBoost are significantly improved from the baseline. This proves that the proposed method predictions give more accurate prediction results and can avoid prediction mistakes in the DFM. A comparative analysis is performed on the other proposed blockchain-based approaches for handling ePrescriptions. Results from the Analysis are shown in Table IV. As we can see compared to the other state-of-art, FortiRx 2.0 is the only solution that combines blockchain-based ePrescription management and a Federated approach for prescription drug forecasting.

TABLE III

LOSS AND MSE EVALUATION METRICS OF IMPLEMENTED FEDERATED LEARNING COMPARED TO BASELINE MODELS FOR EACH DRUG TYPE

Method	Metric	M01AB	M01AE	N02BA	N02BE	N05B	N05C	R03	R06
Naive	Loss	415.830	375.466	267.550	2042.151	629.400	162.000	1168.250	329.200
Naive	MSE	116.014	93.875	44.741	2753.643	255.485	14.920	948.560	82.228
Seasonal Naive	Loss	449.310	511.552	301.250	3530.317	699.800	166.000	1218.1666	596.570
Seasonal Naive	MSE	137.699	197.862	58.105	8829.751	294.693	17.760	1068.780	250.794
Federated XGBoost	Loss	0.860	0.542	0.695	22.760	2.718	0.133	17.702	1.304
Federated XGBoost	MSE	50.073	52.774	41.403	1346.836	161.162	7.845	1044.049	76.623

TABLE IV

COMPARATIVE ANALYSIS OF PROPOSED FORTIRX 2.0 WITH THE STATE-OF-ART

Parameter	S.V. Ionescu et al. [9]	VigilRx [10]	FortiRx [5]	**FortiRx 2.0 (Current Paper)**
Blockchain Platform	Ethereum	Ethereum	Ethereum	Ethereum
Prescription Privacy	Asymmetric Encryption	Role-Based Access Control	Role-Based Access Control and CP-ABE	Role-Based Access Control and CP-ABE
Data Management	On-chain	On-Chain	On-chain and Off-chain	On-chain and Off-chain
Prescription Drug Demand Forecasting	✗	✗	✗	✓

VII. CONCLUSION AND FUTURE RESEARCH

Proposed FortiRx 2.0 utilizes blockchain-based prescription system FortiRx for prescription management which ensures reliable data is made available to the DFM model. This real-time data can help in efficiently training the DFM which can avoid the prediction mistakes in Pharmaceutical Product Demand. The Federated XGBoost method also ensures the privacy of the patients by not sharing datasets with the centralized server and training local models. Accurate production of demand for pharmaceutical products can also avoid the Bullwhip effect in the supply chains and address the disruptions from inaccurate demand predictions. The proposed method is implemented using the Flower framework for leveraging federated learning and loss, and MSE regression metrics are computed. These computed metrics are compared with commonly used baseline models like Naive and Seasonal Naive. This comparative analysis has shown that the proposed method is efficient and has resulted in lower Loss and MSE compared to baseline. Hence, the proposed FortiRx 2.0 not only improves the data quality for DFM while providing data security and privacy.

In future work, more advanced models will be explored to improve the performance of the proposed system. The performance of the proposed system can also be improved significantly by considering multivariate time series analysis with more exploratory attributes such as location, price of drug, weather conditions, etc.

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