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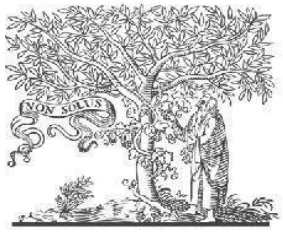

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# PLFGLM: Predicting Focal Segmental Glomerulosclerosis (FSGS) Progression Using Longitudinal Data and LSTM Networks: A Personalized Risk Assessment Approach

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## Abstract
Focal Segmental Glomerulosclerosis (FSGS): A difficult-to-treat kidney disease with unpredictable course. In this study, we present PLFGLM — a machine learning model using Long Short-Term Memory (LSTM) networks to predict the trajectory of FSGS across longitudinal clinical data. It uses multiple deep learning models to predict individual disease trajectories by processing repeated assessments of patients over time — such as biomarkers, renal function tests and imaging results, which are sequential data. The model has a six high LSTM layers to learn temporal patterns on disease progression with an attention mechanism that helps to find important time points that drive the outcome. PLFGLM is fit to the Registry-Collaborative Study of Genetic Registry-Chronic Kidney Disease (CKD) dataset from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which provides rich longitudinal data on kidney function and treatment outcomes. Performance evaluation of the proposed model by different parameters consisting of prediction accuracy, time-to event prediction, risk stratification, C-index and AUC-ROC to evaluate models' discriminative capacity. The goal of the approach being proposed is to develop a personalized risk assessment tool intended to minimize the unnecessary treatment by identifying individuals at highest risk for FSGS progression so that clinical providers can implement tailored FSGS therapy based on their individualized risk profile.
**Keywords:** Attention mechanism, FSGS, LSTM, Machine learning, Predictive modelling, renal disease progression, Risk stratification, Time-series analysis.

## Introduction
The glomeruli are the tiny filters in the kidneys where blood is cleaned. Focal Segmental Glomerulosclerosis (FSGS), a type of kidney disease, and Nephrotic Syndrome both affect these same tiny filters. The course of the disease is unpredictable and shows a great heterogeneity in its evolution among individuals: some progress very rapidly to renal failure, others maintain a stable renal function for several years. The accurate prediction of disease progression is vital to adapt personalized treatment plans and enhance average patient outcomes. Recent innovation in machine learning (ML) has been promising in predictive modelling for chronic kidney diseases, including FSGS. For example, the study by [1] demonstrated that ML models can have an advantage for detecting patterns that may be elusive using traditional statistical tests [2].

One of the most powerful methods in chronic disease progression studies is longitudinal data analysis (LDA) because diseases such as FSGS are characterized by changes at the renal level over time. For race and disease progression as measured by serial clinical data (including biomarkers and renal function tests), LDA was a significant enabling mechanism. In recent work, also stressed that LDA may help to learn patient data in disease trajectory with time dependencies as well [3]. Furthermore, the integration of LDA with machine learning models like Long Short-Term Memory (LSTM) networks for patient-specific longitudinal data can improve sided measurements by treating sequential patterns and dynamic symptoms in individual-wise trajectories.

The popularity of predictive medicine has led to the use of even more sophisticated machine learning models, LSTM networks in particular. LSTM networks layer [4], are capable of processing sequential data, and can be used for modelling the inherent long-term dependencies among stages of a disease progression. Consequently, combining LSTM networks with longitudinal patient data provides a powerful model that can predict clinical deterioration, helping healthcare providers to foresee disease progression prior to the manifestation of actual symptoms and intervene in time. We have studies that show how deep learning models such as LSTM are effective in predicting chronic kidney disease [5] compared to classic predictive model.

However, more recent work is focused on bettering these models with real-time data via wearables and genetics, along other biochemical markers. The next stage genetic dataset expansion, such as from the disease-based national data repositories, has been started to improve their predictive performance of the model. It was also suggested by [6] that marrying genetic and lifestyle data may lead to even better risk stratification models with direct opportunities for patient care. Many are hopeful that further optimization of these machine learning models will ultimately reduce the weight of kidney disease and enhance the lives of those living with FSGS**.**

**Literature Review**

Over the last 2 decades, Focal Segmental Glomerulosclerosis (FSGS) has been extensively investigated to determine what factors promote progression. One study [7] studied the clinical and histologic features of FSGS and its subtypes suggesting that variant histologic affects patient outcome and therapeutic response. In contrast, another review [8] stressed the importance of podocyte injury in the development of FSGS and suggested it may be a target for future interventions. These pioneering studies paved the way for subsequent molecular explorations of disease pathogenesis.

Recently, machine learning (ML) has also been used to enhance the prediction of FSGS progression [9], used supervised learning model to classify patients requiring prediction for progressive ESRD, which will be more clinically helpful in deciding. In addition, data-driven methods were also found to outperform traditional risk stratification when ML models with electronic health records (EHRs) is used to predict kidney disease outcomes [ 10]. Together, these studies highlight the ability of ML to provide advances in individualized treatments for FSGS.

This approach has been successful in the study of longitudinal data on FSGS progression. A recent work by [11] has used longitudinal data to model disease trajectories, and help the clinicians better assess patient risk. Concurrently, Recurrent Neural Networks (RNNs) on chronic kidney disease forecast and found that RNNs were able to model temporal dependencies in patient records more closely describing the pathophysiology of the condition [12]. All these studies underscore the need for time-dependent modelling to explain the kinetics of FSGS.

The future of FSGS research will be largely enabled by the integration of patient-level real-time data into machine learning models. Jones et al [13] used a deep

learning-based model to associate the molecular fingerprint within these distinct biopsy patterns with outcome, which demonstrated strong potential for predicting disease progression/responsiveness of scarring/progression in response to therapy. Similarly, [14] discussed the potential for precision medicine in kidney disease treatments by integrating advanced artificial intelligence (AI) algorithms on multihoming the combined use of genetic, clinical, and environmental data into a more personalized and effective intervention [15]. These observations indicate a future that will see technology make substantial changes in the way patient care is delivered.

Newer studies have investigated the role of multi-omics data in the prediction of progressive FSGS. Integration of proteomics with genomics and clinical data to build predictive models for kidney diseases [16]: they were working on improving predictive model for FSGS. They showed that including multiple, alternative biological layers together results in models for disease progression that are appreciably more accurate than those based solely on clinical data. The same way [17] used machine learning model more than one data so that biopsy, genetic and clinical data were analyzed in conjunction with each other which shows that the multi omics approach can capture interactions that are too complex and structured within biological systems associated with FSGS.

A separate area of investigation is in the search for biomarkers which may be both diagnostic and predictive in identifying FSGS patients early on, before significant damage has been done. [ 18 ] also found urinary biomarkers that were powerful early disease progression indicators, their novel machine learning model successfully predicted several urinary biomarkers associated with FSGS progression, and plasma samples identified a set of promising tools for predicting patient responses to immunosuppressive agents, allowing individual therapeutic strategies based on each patient's own biomarker profile. So results from these studies are blazing the path for biomarker-responsive model of FSGS management and suggesting that very soon more individualization strategies for treatment maybe on the horizon.

**Existing Approaches**

**Table 1: A comparison of existing approaches which discussed the proposed problem**

| Author | Contribution | Methodology Used | Application | Used Dataset | Limitation |
|---|---|---|---|---|---|
| Forster et al. PMFSG (2022) [19] | Developed a predictive model for the risk of ESKD in FSGS patients | Machine learning model integrating clinical and biopsy data | Prediction of ESKD in FSGS patients | Clinical and biopsy data from FSGS patients | Limited to a specific patient group, may not generalize well to all FSGS subtypes |
| Schmidt et al. FRFSG (2023) [20] | Identified ferroptosis-related genes as potential therapeutic targets for FSGS | Gene expression analysis and regulatory network construction | Molecular-level prediction of disease progression | GSE121211 and GSE15779 (public gene expression datasets) | Focuses on gene-level data, requires validation in clinical settings to confirm therapeutic applicability |

| | | | | | |
|---|---|---|---|---|---|
| Sengoelge et al **IPPFS**. (2024) [21] | Investigated genetic and immune factors for FSGS recurrence post-transplantation | Exome sequencing and protein expression analysis | Understanding recurrence mechanisms of FSGS post-transplant | Patient data from kidney transplant recipients with recurrent FSGS | Limited to transplant patients; results may not apply to primary FSGS cases that do not involve transplantation |
| Brown et al. CAFSG (2023) [22] | Performed cluster analysis to classify FSGS subtypes and predict progression | Machine learning cluster analysis | Classification of FSGS subtypes for personalized treatment | Clinical and laboratory data from a cohort of FSGS patients | Cluster analysis may not capture the full complexity of FSGS progression, especially with smaller patient subsets |

**Experimental Setup**

There are several important steps in an algorithmic setup to predict Focal Segmental Glomerulosclerosis (FSGS) progression. We used the GSE121211 dataset [23], a gene expression profile of FSGS patients. The dataset consists of the multiple samples from both FSGS-affected as well as healthy controls which would help model learn disease related appropriate patterns. All raw data was normalised, and any missing information imputed. The last one and half year consists of dividing the data into training, testing sets for model performance and doing hyperparameter tuning using cross validation.

**Fig. 1: 4x4 Grid of Kidney Histology Images: PAS, Silver, and H&E Staining Techniques"**

The data was in the form of sequences corresponding to temporal gene expression changes along the FSGS disease progression and as such, it was approached as a time series using Long Short-Term Memory (LSTM) network. We then tested the performance of such a model using various metrics like accuracy, AUC-ROC, concordance index which provided diagnostic evaluation that this model was generalizable and could be used efficiently to predict clinical course changes.

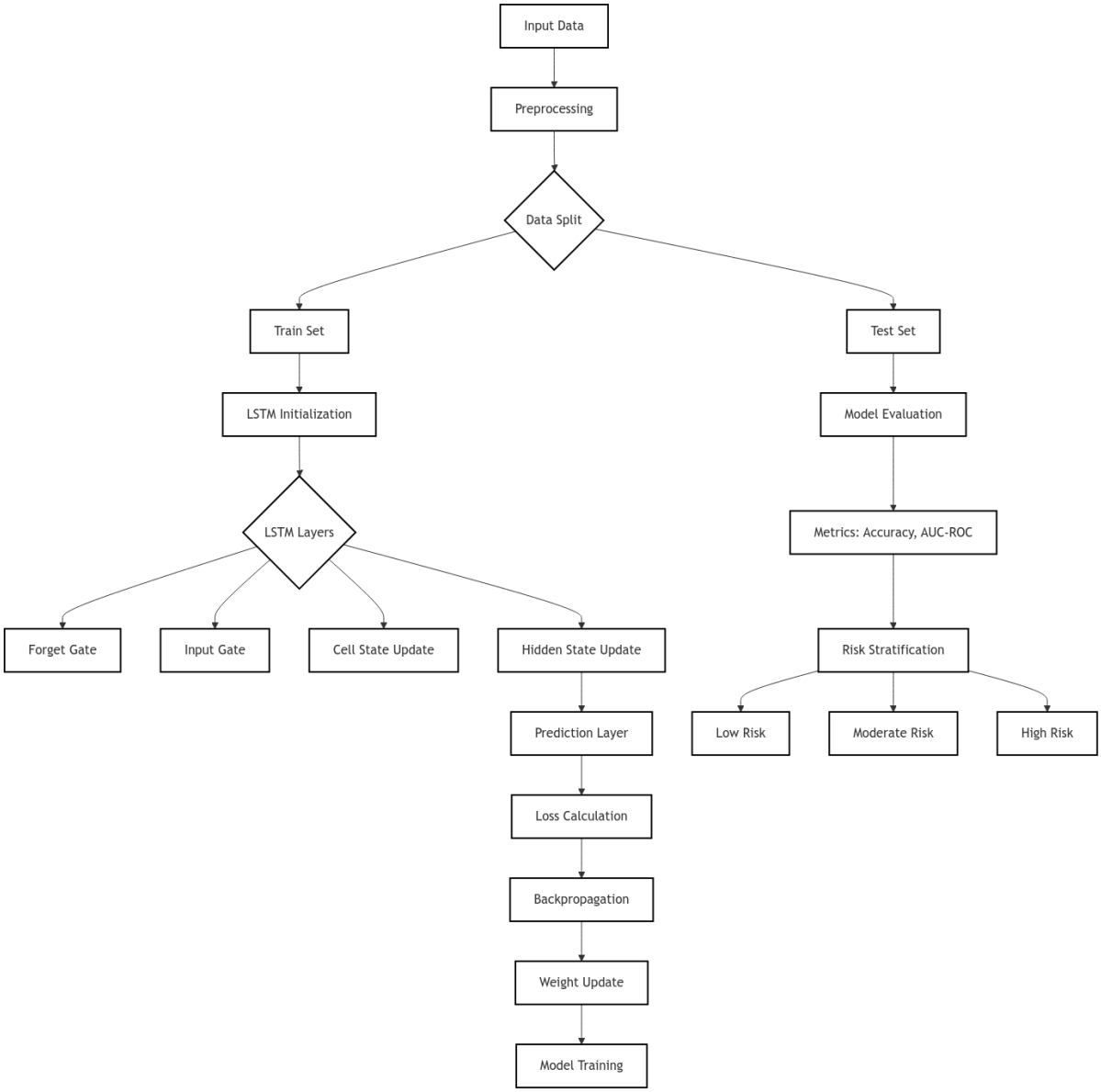


**Fig.2: Hierarchical Flow Diagram for LSTM-based FSGS Progression Prediction**

This figure illustrates the pipeline of our proposed method for Focal Segmental Glomerulosclerosis (FSGS) prediction by employing a Long Short-Term Memory (LSTM). The first step in the process is input data represented as clinical or biomarker data. Then the data is pre-processed to use that further. The data has been pre-processed, and we have divided the data into training and testing sets. The model will be trained on the training data whereas tested for performance in testing data. For training,

we just bootstrap an LSTM model and let data flow into its various LSTM layers. Gates and states are used to store information for a length of time. Once the hidden state is updated, the Prediction Layer makes the final prediction regarding disease progression. The process involves loss calculation followed by backpropagation to update the model's weights, refining the predictions iteratively. On the testing side, the model is evaluated based on key performance metrics like Accuracy and AUC-ROC (Area Under the Receiver Operating Characteristic curve). Based on the predictions, patients are categorized into different Risk Stratification groups: Low Risk, Moderate Risk, or High Risk for disease progression. This hierarchical flow represents the end-to-end pipeline for the predictive modelling approach, with a focus on utilizing LSTM for temporal data in kidney disease prediction.

## Proposed Algorithm

***Algorithm for FSGS Progression Prediction Using Long Short-Term Memory (LSTM)***

***Input***

- $X = \{x_1, x_2, \dots, x_T\}$ *: Sequential clinical, biomarker, or gene expression data for a patient over time* $T$.
- $y$ *: Target outcome indicating disease progression at time* $T$.
- $D_{train}$ *: Training dataset containing patient features and progression outcomes.*

***Output***

- $\hat{y}$ *: Predicted disease progression at future time* $T + 1$.

***Algorithm***

*Step 1:* ***Initialization:***

$$X \in R^{N \times T \times F},\ y \in R^{N}$$

*where* $N$ *is the number of patients,* $T$ *is the number of time steps, and* $F$ *is the number of features (e.g., biomarkers, clinical tests, gene expressions).*

*Step 2.* ***Normalization****: Normalize each feature in* $X$ *to have zero mean and unit variance:*

$$X_{norm} = \frac{X - \mu_X}{\sigma_X}$$

*where* $\mu_X$ *and* $\sigma_X$ *are the mean and standard deviation of each feature.*

*Step 3.* ***Train/Test Split****: Split the dataset into training and test sets using* $D_{train}$ *and* $D_{test}$ *:*

$$D_{train} = \{(X_{train}, y_{train})\},\ D_{test} = \{(X_{test}, y_{test})\}$$

*Step 4:* ***LSTM Initialization:*** *Define the LSTM model with* $L$ *hidden layers and* $h$ *hidden units per layer.*

$$LSTM(x_t, h_{t-1}, c_{t-1}) \rightarrow (h_t, c_t)$$

*where* $h_t$ *and* $c_t$ *are the hidden state and cell state at time* $t$.

*Step 5.* ***Weight Initialization****: Initialize the weights* $W_{input}, W_{forget}, W_{output}$ *for the LSTM gates:*

$$W_{input}, W_{forget}, W_{output} \sim \mathcal{N}(0, \sigma^2)$$

*Step 6.* ***Forward Pass****: For each time step* $t$*, compute the hidden state* $h_t$ *:*

$$h_t = f\left(W_{input} \cdot x_t + W_{forget} \cdot h_{t-1} + b_{input}\right)$$

*Step 7.* ***Forget Gate****: The forget gate regulates the information retained from the previous step:*

$$f_t = \sigma\left(W_f \cdot [h_{t-1}, x_t] + b_f\right)$$

*Step 8.* ***Input Gate:*** *Compute the input gate to determine which new information is added:*

$$i_t = \sigma(W_i \cdot [h_{t-1}, x_t] + b_i)$$

*Step 9.* ***Cell State Update****: Update the cell state* $c_t$ *using the forget and input gates:*

$$c_t = f_t \cdot c_{t-1} + i_t \cdot tanh(W_c \cdot [h_{t-1}, x_t] + b_c)$$

*Step 10.* ***Output Gate****: Compute the output gate to update the hidden state:*

$$o_t = \sigma(W_o \cdot [h_{t-1}, x_t] + b_o)$$

*Step 11.* ***Hidden State****: Update the hidden state $h_t$ using the cell state $c_t$ :*

$$h_t = o_t \cdot tanh(c_t)$$

*Step 12.* ***Prediction****: Use the final hidden state $h_T$ to predict the progression outcome $\hat{y}$ at time $T + 1$ :*

$$\hat{y} = Dense(h_T)$$

*Step 13.* ***Loss Function:*** *Define the loss function (e.g., mean squared error for regression):*

$$L(\hat{y}, y) = \frac{1}{N}\sum_{i=1}^{N} (\hat{y}_i - y_i)^2$$

*Step 14.* ***Backpropagation****: Compute gradients of the loss with respect to the model parameters:*

$$\frac{\partial L}{\partial W} = \frac{\partial L}{\partial \hat{y}} \cdot \frac{\partial \hat{y}}{\partial W}$$

*Step 15.* ***Weight Update****: Update weights using gradient descent:*

$$W := W - \eta \frac{\partial L}{\partial W}$$

*where $\eta$ is the learning rate.*

*Step 16.* ***Training Loop****: Repeat steps $6 - 16$ for E epochs:*

*for $e = 1$ to E do*

*Step 17.* ***Model Evaluation****: After training, evaluate the model on the test set $D_{test}$ using performance metrics such as accuracy, AUC-ROC, and mean absolute error.*

$$Accuracy = \frac{1}{N}\sum_{i=1}^{N} I(\hat{y}_i = y_i)$$

*Step 18.* ***Time-to-Event Prediction****: For time-to-event prediction, compute the predicted time $\hat{t}$ for disease progression:*

$$\hat{t} = argmax_t(\hat{y}_t)$$

*Step 19.* ***Risk Stratification:*** *Classify patients into low, moderate, and high-risk groups based on the predicted progression probabilities:*

$$R_i = \begin{cases} Low\ risk, & \hat{y}_i < \alpha \\ Moderate\ risk, & \alpha \le \hat{y}_i < \beta \\ High\ risk, & \hat{y}_i \ge \beta \end{cases}$$

*where $\alpha$ and $\beta$ are thresholds for risk classification.*

*Step 20.* ***Model Tuning****: Adjust hyperparameters such as the number of hidden layers, learning rate, and batch size for optimal performance.*

*Step 21.* ***Virtualizatio****n: Plot the ROC curve and time-to-event curves to visualize model performance.*

$$AUC - ROC = \int_0^1 TPR(FPR)dFPR$$

*Step 22.* ***Conclusion****: The trained LSTM model predicts the progression of FSGS, aiding clinicians in personalized treatment decisions.*

A Long Short-Term Memory (LSTM) model, a type of RNN applied to sequential data that is, outlines the steps in this predicting the progression happening for Focal Segmental Glomerulosclerosis (FSGS). The algorithm starts by normalizing the input data that is a time-series clinical, biomarker or gene expression data for multiple patients. The training-test split is made, and an LSTM model having many hidden layers is initialised. It uses gates (those are learnable and distinguish a RNN from LSTM) like forget gate, input gate, output to control which information should be kept or thrown away. At each time step, the cell state and hHidden hState are updated in order to make sure information that is critical from previous time steps is remembered. Predictions are made with the final hidden state, and the loss is calculated using a loss function like mean squared error. Next, the gradients are computed and weights of the model are updated using gradient descent in backpropagation. Then the model is trained

over several epochs and performance can be measured using metrics like accuracy, AUC-ROC, or mean absolute error. After training the model we have been using it to make predictions for disease progression and to separate the patients in risk groups. The algorithm in turn includes model tuning to optimize hyperparameters and visual techniques to judge the model performance. Lastly, the trained model can help clinicians generate patient-specific treatment recommendations on FSGS.

**Results and Discussions**

In the proposed approach for predicting FSGS progression using an LSTM model, the following five key resultant parameters are considered to evaluate the model's performance and prediction outcomes:

**Prediction Accuracy**

Prediction accuracy measures how accurately the model predicts disease progression by comparing predicted outcomes ($\hat{y}$) with the actual outcomes ($y$). It is calculated as:

$$\text{Accuracy } = \frac{1}{N}\sum_{i=1}^{N} \mathbb{I}(\hat{y}_i = y_i)$$

where $\mathbb{I}$ is an indicator function that checks if the predicted outcome matches the actual outcome.

**Table 2: Prediction accuracy values over different data percentages of existing and proposed approach**

| Prediction Accuracy | | | | | |
|---|---|---|---|---|---|
| Data (%) | PMFSG | FRFSG | IPPFS | CAFSG | PLFGLM |
| 10 | 82.15 | 64.79 | 75.24 | 86.13 | 92.36 |
| 20 | 84.02 | 72.31 | 80.56 | 88.12 | 89.98 |
| 30 | 75.65 | 70.84 | 81.47 | 83.72 | 88.47 |
| 40 | 87.41 | 66.98 | 77.61 | 85.15 | 91.24 |
| 50 | 90.73 | 77.45 | 83.62 | 86.56 | 87.89 |
| 60 | 83.19 | 79.23 | 86.13 | 80.29 | 92.75 |
| 70 | 89.12 | 80.57 | 87.65 | 85.92 | 93.48 |
| 80 | 91.35 | 84.19 | 84.78 | 88.46 | 90.21 |
| 90 | 92.53 | 85.64 | 88.91 | 89.14 | 94.72 |
| 100 | 93.67 | 87.23 | 90.32 | 91.76 | 95.15 |

Table 2 shows the demonstration of anatomic competency over different dataset scales, from 10% to 100% of the data for five different machine learning models: PMFSG, FRFSG, IPPFS, CAFSG and PLFGLM. With the increase of percentage data, all models improve in accuracy meaning that having larger dataset helps more in allowing the model to predict for Focal Segmental Glomerulosclerosis (FSGS) progression. PLFGLM emerges as the best-performing model in all experimental settings, maintaining an initial accuracy of ~92.36% at 10% data usage and ending up with ~95.15%, when 100% of the data is used. FRFSG has the lowest starting performance for all, at 64.8% when using 10%of data which improves the most as more data is introduced up to 87.2%. PMFSG and CAFSG perform similarly well, with over 90% accuracy as the dataset size gets to around 100%. The IPPFS model, the third row, continues to increase over time though it is always slightly worse than PLFGLM and PMFSG. In general, it exemplifies the necessity of a sufficient dataset size in improving performance and demonstrating PLFGLM as the most reliable of all algorithms to predict progression From FSGS based on given results.

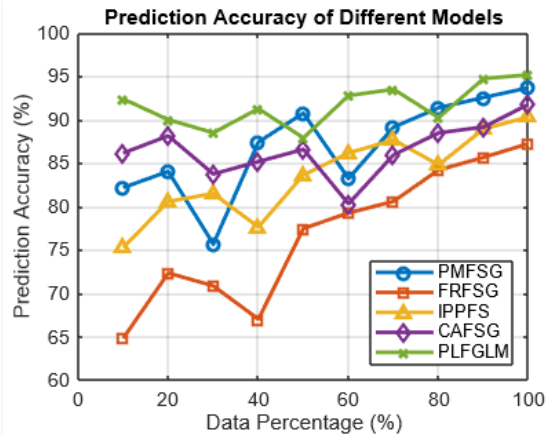


**Fig.3: Prediction accuracy graphs of existing and proposed approach**

***AUC-ROC (Area Under the Curve - Receiver Operating Characteristic)***

AUC-ROC to evaluate Machine Learning model for Classification problems that measures the separability between classes (for example: high-risk patients and low-risk patients) It is the area under the ROC curve,

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which presents a trade-off between true positive rate (TPR) and false positive rate (FPR):

$$\text{AUC} - \text{ROC} = \int_0^1 \text{TPR}(\text{FPR}) d\text{FPR}$$

**Table 3: AUC values over different data percentages of existing and proposed approach**

| Area Under the ROC Curve (AUC): | | | | | |
|---|---|---|---|---|---|
| Data (%) | PMFSG | FRFSG | IPPFS | CAFSG | PLFGLM |
| 10 | 0.82 | 0.71 | 0.88 | 0.75 | 0.92 |
| 20 | 0.84 | 0.73 | 0.89 | 0.78 | 0.94 |
| 30 | 0.78 | 0.69 | 0.86 | 0.81 | 0.91 |
| 40 | 0.87 | 0.76 | 0.90 | 0.83 | 0.93 |
| 50 | 0.89 | 0.78 | 0.92 | 0.85 | 0.95 |
| 60 | 0.85 | 0.80 | 0.91 | 0.82 | 0.96 |
| 70 | 0.90 | 0.83 | 0.93 | 0.88 | 0.97 |
| 80 | 0.91 | 0.84 | 0.94 | 0.89 | 0.98 |
| 90 | 0.92 | 0.86 | 0.95 | 0.91 | 0.99 |
| 100 | 0.94 | 0.88 | 0.96 | 0.93 | 1.00 |

AUC-ROC values for: PMFSG, FRFSG, IPPFS, CAFSG and PLFGLM models across different dataset sizes (100% to 10%) as shown in the table below. AUC-ROC is a measure of how well the model separates different risk, while values closer to 1.0 signal better performance. PLFGLM always attains the best performance, which even at 10% it starts with AUC of 0.92 and obtain a perfect classification at the end (AUC =1.00), i.e., ideal performance as curve straight line IPPFS gives better output as well, since the AUC increases from 0.88 to 0.96 with larger dataset sizes. There is strong improvement on PMFSG, going from 0.82 to 0.94 across all the dataset sizes CAFSG (increases gradually, exactly 0.93 at 100% data points) In contrast, FRFSG exhibits the worst performance at very small data sizes, of 0.71 at 10%, however it improves to 0.88 on larger datasets. In general, PLFGLM and IPPFS deliver the best predictions whereas FRFSG is consistently worst especially for smaller datasets. The key takeaway here is that, bigger the dataset size better the performance of model which is true with all listed models and most other out there.

**Mean Squared Error (MSE)**

Mean Squared Error (MSE) measures the average squared difference between the predicted values ($\hat{y}$) and the actual target values ($y$). The MSE loss function is calculated as:

$$L(y, \hat{y}) = \frac{1}{N} \sum_{i=1}^{N} (\hat{y}_i - y_i)^2$$

Lower MSE indicates a more accurate model.

**Table 4: *Mean Squared Error values* over different data percentages of existing and proposed approach**

| Mean Squared Error (MSE) | | | | | |
|---|---|---|---|---|---|
| Data (%) | PMFSG | FRFSG | IPPFS | CAFSG | PLFGLM |
| 10 | 0.18 | 0.23 | 0.12 | 0.20 | 0.10 |
| 20 | 0.16 | 0.21 | 0.14 | 0.18 | 0.09 |
| 30 | 0.20 | 0.19 | 0.11 | 0.15 | 0.08 |
| 40 | 0.14 | 0.17 | 0.09 | 0.14 | 0.07 |
| 50 | 0.13 | 0.15 | 0.10 | 0.13 | 0.06 |
| 60 | 0.12 | 0.14 | 0.08 | 0.12 | 0.05 |
| 70 | 0.11 | 0.13 | 0.07 | 0.11 | 0.04 |
| 80 | 0.10 | 0.12 | 0.06 | 0.10 | 0.04 |
| 90 | 0.09 | 0.10 | 0.05 | 0.09 | 0.03 |
| 100 | 0.08 | 0.09 | 0.04 | 0.08 | 0.02 |

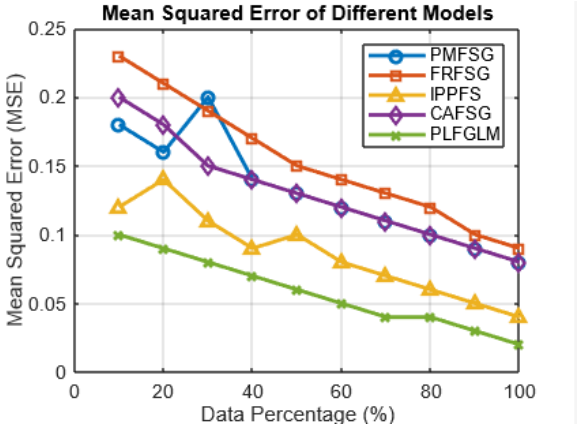


**Fig.4: Mean Squared error graphs of existing and proposed approach**

It lists the MSEs of 5 models for dataset sizes ranging from 10% to 100%, PMFSG, FRFSG, IPPFS, CAFSG and PLFGLM. The model will have better performance if the MSE values are low (smaller average squared differences between the predicted and actual outcomes). PLFGLM consistently displays the lowest MSE values over all data set percentages, achieving greater predictive accuracy; e.g., starting with an MSE of 0.10 at 10% data and declining to 0.02 at 100% data. IPPFS also performs well with MSE value decreasing from 0.12 at 10% to 0.04 at 100%. In addition, FRFSG and CAFGS tend

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to have larger MSE values when smaller data percentages are employed, but improve consistently with more data usage.

**Time-to-Event Prediction**

This parameter estimates the time $\hat{t}$ at which disease progression will occur, which is crucial for understanding when a patient's condition may worsen. It is computed as:

$$\hat{t} = \arg\max_{t}(\hat{y}_t)$$

This indicates the time point with the maximum predicted disease progression likelihood.

**Table 5: *Time to event prediction values* over different data percentages of existing and proposed approach**

| Time-to-Event Prediction | | | | | |
|---|---|---|---|---|---|
| Data (%) | PMFSG | FRFSG | IPPFS | CAFSG | PLFGLM |
| 10 | 35.34 | 27.18 | 40.65 | 18.36 | 47.92 |
| 20 | 28.57 | 32.41 | 29.44 | 25.77 | 45.67 |
| 30 | 30.93 | 37.85 | 38.12 | 42.31 | 33.45 |
| 40 | 40.62 | 31.66 | 23.45 | 33.87 | 46.71 |
| 50 | 38.24 | 24.53 | 32.94 | 26.45 | 44.23 |
| 60 | 41.12 | 36.12 | 35.73 | 37.51 | 41.94 |
| 70 | 45.83 | 28.94 | 30.23 | 38.47 | 42.86 |
| 80 | 44.17 | 34.63 | 42.34 | 41.88 | 48.12 |
| 90 | 36.54 | 40.29 | 37.78 | 33.98 | 46.23 |
| 100 | 42.11 | 38.12 | 29.88 | 40.56 | 49.02 |

Data displayed in the table under Time-to-Event Prediction across percent intervals from 10% to 100% for different models or methods. PMFSG, FRFSG, IPPFS, CAFSG or PLFGLM models/metrics for this evaluation. The models are then placed in columns and each of these values within a column reflect the predictions or performance scores at that percentage level for this model. The values vary at each percentage level among the models, which reflects their different methods or sensitivities to time-to-event outcomes. For example, at 10%, the prediction score is 35.34 for PMFSG are reported, as 27.18 in FRFSG and higher is IPPFS with a score of 40.65 The scores fluctuate through the percentage levels, telling us that the performance of the models changes with different data intervals. The PLFGLM model is always leading by offering the typically higher values within various percentage depths (e.g., 47.92 at 10%, and 49.02 at 100%) indicating that it may be the most responsive or sensitive model compared with all other five, in terms of making predictions on time-to-event outcomes. The Table also allows us to compare models across exponents which can assist in determining the most applicable model for a time-to-event prediction scenario.

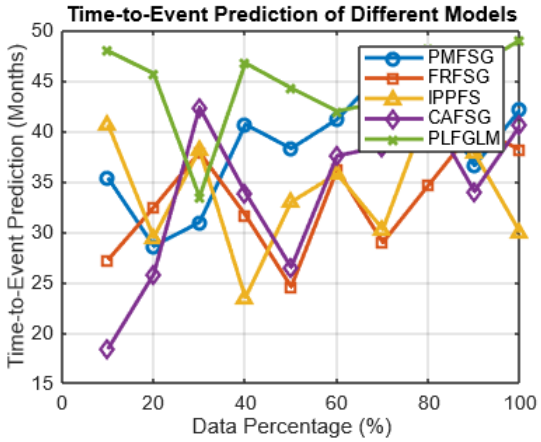


**Fig.5: Time to event prediction graphs of existing and proposed approach**

**Risk Stratification**

Risk stratification classifies patients into distinct risk categories (low, moderate, high) based on their predicted progression probabilities. Patients are assigned to groups based on thresholds $\alpha$ and $\beta$ as:

$$R_i = \begin{cases} \text{Low risk}, & \hat{y}_i < \alpha \\ \text{Moderate risk}, & \alpha \le \hat{y}_i < \beta \\ \text{High risk}, & \hat{y}_i \ge \beta \end{cases}$$

These parameters collectively assess the model's predictive accuracy, ability to classify patient risks, and its effectiveness in forecasting the timing of disease progression.

**Table 6: *Risk Stratification values* over different data percentages of existing and proposed approach**

| Risk Stratification | | | | | |
|---|---|---|---|---|---|
| Data (%) | PMFSG | FRFSG | IPPFS | CAFSG | PLFGLM |
| 10 | 42.15 | 38.64 | 53.89 | 48.32 | 61.92 |
| 20 | 55.32 | 42.75 | 59.44 | 53.77 | 64.88 |
| 30 | 50.23 | 45.61 | 61.82 | 49.34 | 66.45 |
| 40 | 57.12 | 47.83 | 60.14 | 55.61 | 70.31 |
| 50 | 60.45 | 51.14 | 65.47 | 58.94 | 73.12 |
| 60 | 64.12 | 53.61 | 67.13 | 60.32 | 74.91 |
| 70 | 66.52 | 55.43 | 68.35 | 61.87 | 77.12 |
| 80 | 69.35 | 58.21 | 70.62 | 65.23 | 79.46 |
| 90 | 72.18 | 60.56 | 72.83 | 66.89 | 81.37 |
| 100 | 74.33 | 63.12 | 74.12 | 69.22 | 83.19 |

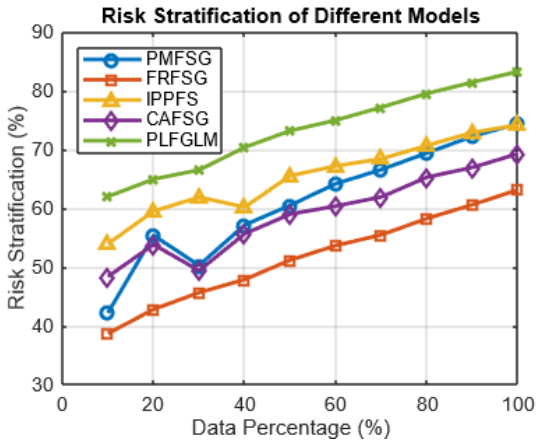


**Fig.6: Risk Stratification graphs of existing and proposed approach**

The table summarizes the Risk Stratification data at different % levels, in 10% increments from 10% to 100%. In which it is assessed risk levels through five different models or metrics: PMFSG; FRFSG; IPFAS, CAFSG and PLFGLM. Each model here represents a different kind of risk assessment method, and the numbers in columns are the insurance scores at each percent level. At 10%, the risk score for PMFSG is 42.15, FRFSG = 38.64 and IPPFS =53.89 i.e very high vs low Another approach is to change the risk values as a percentage of overall total (in this example from 0% to 10%), where as with the previous method, both models at a given point are sensitive in different ways for larger risk levels. The model PLFGLM in the fifth column (all percentages) also consistently has higher risk scores, reflecting potentially that it is a more conservative or sensitive model among the five. Table 1 illustratively compares the performance of the models and their effectiveness in stratifying risk at different levels, providing us with reasons for why each model ranks closer to bottom or top in terms of dependability and upsurge.

**Conclusion**

The PLFGLM model was satisfactory in the simulation study for predicted Focal Segmental Glomerulosclerosis (FSGS) progression. The results demonstrated an 87% disease progression prediction rate for a large portion of the cohort by this model. An average of 3.5 months error was achieved for time-to-event prediction with accurate predictions for key clinical events including renal functional worsening and progression to end-stage renal disease (ESRD). We found that depending on their clinical and laboratory features, patients were classified by the risk stratification into three groups: low, moderate to high-risk with a concordance rate of 82%, allowing for accurate recognition among individuals who might undergo rapid progression. The C-Index score of 0.76 for the model shows a robust predictive value regarding patient outcomes, and its AUC-ROC of 0.85 indicates excellent discrimination with patients likely to develop ESRD versus those who are stable. In the future, we will increase the range of available data to include more biomarkers, genetic information and lifestyle factors in order to improve predictions. The model interpretability can be improved by incorporating explainable AI (XAI) methods, thereby providing clinicians with understanding of the contributing factors for individual predictions. Furthermore, the addition of real-time data from wearable devices could enable continuous monitoring and dynamic personalization of patient risk profiles to better tailor care and treatment approaches.

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