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Mathematical Modeling And Explainable Artificial Intelligence For Multivariate Disease Progression Prediction And Personalized Clinical Decision-Making In General Medicine And General Surgery

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Abstract
Accurate prediction of disease progression is crucial when making early and individualised decisions in general medicine and general surgery where patient condition is dynamic and changes in response to a combination of physiological and clinical factors. Existing risk scores partially capture temporal interactions and largely lack clinical interpretation.Existing risk scores have limited ability to represent temporal interaction, and data-driven risk scores are lacking of clinical interpretation. In this study, we suggest an integrated Mathematical Modeling and Explainable Artificial Intelligence (MM-XAI) framework for multivariate disease-progression prediction and personalized clinical decision support. The clinical state variables associated with each etiology, and which are known to be associated with physiological instability, biochemical abnormality, inflammatory burden, disease severity, and clinical/surgical stress, are modeled with nonlinear temporal dynamics. The resulting progression information is then combined with an AI classifier to distinguish between stable, moderate-risk and high-risk states and to provide explanation of patient-specific predictions using a feature attribution algorithm, SHAP. The performance is assessed by accuracy, sensitivity, specificity, F1-score, AUROC, calibration error, progression prediction error and explanation consistency. The framework extends from patient state to mathematical progression to AI prediction to explanation to personalized decision support to create an interpretable computational framework for risk assessment. Real-world clinical deployment requires prospective multicenter clinical trials to validate in the real world.

Keywords: Mathematical modeling; Explainable artificial intelligence; Disease progression; Clinical decision support; General medicine; General surgery; Personalized medicine.

1. Introduction

Clinical deterioration and disease progression remain a significant challenge in general medicine and general surgery as patients with apparently similar setting can take substantially different clinical courses. Patient health is a truly multivariate phenomenon, and it is affected by multiple factors interacting within the physiology, biochemistry, inflammation, disease and treatment domains. It is possible that these indicators may fluctuate continually throughout the hospital stay, medical management, surgery and recovery. Thus, early detection of unfavorable progression is crucial to recognize high-risk cases and to clinical assessment in early phase before significant deterioration.

Traditional clinical scoring systems offer helpful standardised approximations of patient risk, but are generally derived from predetermined variables, fixed cut points, or variables measured at specific limited points in time. These methods may not capture multi-level and/or dynamic interactions between multiple clinical indicators. This has prompted studies into the use of machine-learning and deep-learning approaches for clinical risk prediction, which leverages multivariate information and provide the capacity to learn complex information relationships. In safety-critical healthcare applications, however, simply having high predictive power is not enough. Black-box predictions may be less transparent and trusted by clinicians when they determine that their patient is a "high-risk" patient.

In the case of representing the evolution and relationship between clinical variables in the disease state, mathematical models offer an interpretable way of doing so while artificial intelligence models allow for flexible learning of nonlinear predictive patterns. They can thus offer complementary benefits when they're combined. This integration is further supported by explainable artificial intelligence (XAI), which numerically ranks the contribution of clinical factors on prediction-by-prediction basis, allowing clinicians to find out which factors are most likely to contribute to an estimated progression risk. This is a big issue if the focus is on personalized assessment, since population-average predictions might not capture the nature of the patient.

Although these advancements have been made, there is one significant gap in the research. Mathematical disease-progression models frequently offer meaningful dynamics that cannot be learned well from data, while AI models achieve a good predictive performance with less clinical rigor and transparency. In addition, the state modeling of the mathematical aspect of a state, prediction of progression, explanation and personalized decision support are often studied in isolation. To fill this void, in this work an integrated MM-XAI framework is proposed that combines a multivariate mathematical representation of patient state, a temporal disease-progression model, a risk-prediction model based on AI, and a general XAI framework for identification of patient-specific contributing factors, alongside a unified, integrated decision-support mechanism that facilitates general medical and surgical risk assessment.

2. Literature Review

Mathematical modelling has been extensively used to describe disease progression by encapsulating interactions between physiological changes, disease severity, therapeutic reactions and time changes [2]. Dynamical-system approaches are an extension of this concept that describe the evolution of clinical states over time giving interpretable representation of the progression trajectories [14]. Conventional risk factors and severity indices are also important in routine clinical care and have been useful in identifying the high-risk patient [1] but may be insufficient in representing nonlinear interactions and individual temporal changes [3].

Machine-learning techniques have increasingly been investigated for patient deterioration prediction using multivariate clinical variables [6]. Deep-learning models also provide the ability to represent complex physiological and laboratory information in a hierarchical structure and have been used to classify risks, make prognosis, and predict outcomes in the field of general medicine [10]. The same methods were used in general surgery for risk assessment, prediction of complications following surgery, and patients to be monitored closely [8]. However, as the degree of predictive ability increases, the degree of interpretability can decrease, especially in complex architectures like neural networks [15].

Explainable AI is therefore crucial to enhance transparency in clinical prediction [7]. Machine learning techniques like feature attribution, SHAP, attention mechanisms, and local explanations can identify the factors that influence a single patient's prediction and can be used to differentiate patient-specific risk factors [11]. Individual risk stratification should consider not only population average risk patterns but also individual clinical features in personalized medicine [9] and these capabilities complement personalized medicine. Clinical decision-support systems can then incorporate these predictions with patient data to help with clinical evaluation and prioritization [13].

However, there are key gaps in interpretability, applicability across patient groups, temporal nature representation and translational potential to clinical practice [4]. A mathematical model can give an understandable dynamic, but not so good nonlinear learning, while an advanced AI model can give a more powerful prediction, but with less understandable reasoning [12]. Another often studied area is the study of progression modeling, AI prediction, explainability, and decision support individually [5]. A combined architecture encompassing mathematical disease-progression modelling, nonlinear artificial prediction, the ability to explain predictions at feature level and clinical decision support at individual level is still required.

3. Methodology

3.1 Multivariate Patient-State Representation and Data Preprocessing

The proposed MM-XAI framework is based on five clinical variables reflecting the physiological instability, biochemical abnormality, inflammatory burden, disease severity and clinical/surgical stress with which each patient is represented. Such variables offer a concise multivariate description of the clinical state of the patient and are the main input variables to disease-progression modeling. They are summarized in Table 1 below for definitions, ranges and clinical interpretations.

Table 1. Definition and Interpretation of Multivariate Clinical Input Variables

Symbol	Clinical Input Variable	Range	Clinical Interpretation
x_1	Physiological Instability Index (PII)	0–1	Represents deviations in vital physiological indicators such as heart rate, blood pressure, respiratory rate, and oxygen saturation.
x_2	Biochemical Abnormality Index (BAI)	0–1	Quantifies abnormalities in relevant laboratory and biochemical measurements.
x_3	Inflammatory Burden Index (IBI)	0–1	Represents the degree of systemic inflammatory activity based on available inflammatory indicators.
x_4	Disease Severity Index (DSI)	0–1	Describes the overall severity and progression status of the underlying clinical condition.
x_5	Clinical/Surgical Stress Index (CSSI)	0–1	Represents physiological stress associated with treatment, surgical procedures, or clinical interventions.

At a given time t, the multivariate clinical condition of a patient is represented by the patient-state vector

$$x(t) = [x_1(t),\ x_2(t), x_3(t), x_4(t), x_5(t)]^T, \quad (1)$$

Because clinical measurements can have different numerical scales, min-max normalization is applied to transform each variable into the interval $[0,1]$:

$$\tilde{x}_i(t) = \frac{x_i(t) - x_i^{min}}{x_i^{max} - x_i^{min} + \in}, \quad (2)$$

Where x_i^{min} and x_i^{max} represent the minimum and maximum values of the corresponding clinical variable, respectively, and $\in$ is a small constant introduced to prevent numerical instability. Incorporating values near zero reflect relative normality, while values closer to 1 show relative clinical abnormality, severity or stress.

The normalized variables are then combined to calculate a composite clinical severity score:

$$S(t) = \sum_{i=1}^{5} w_i\ \tilde{x}_i(t), \qquad \sum_{i=1}^{5} w_i = 1, \quad (3)$$

where w_i denotes the relative contribution assigned to the i -th clinical variable. The resulting $S(t)$ provides a unified representation of the overall clinical severity while retaining the individual variables for subsequent multivariate progression analysis.

The entire sequence of the processing is shown in Fig. 1. Then, the normalized patient-state vector and composite severity score are passed to the mathematical model of disease progression for a prediction of disease risk using AI, feature attribution using XAI, and personalized clinical decision support. This sets the general

computational channel from the different clinical data to patient-specific meaningfully interpretable risk assessment.

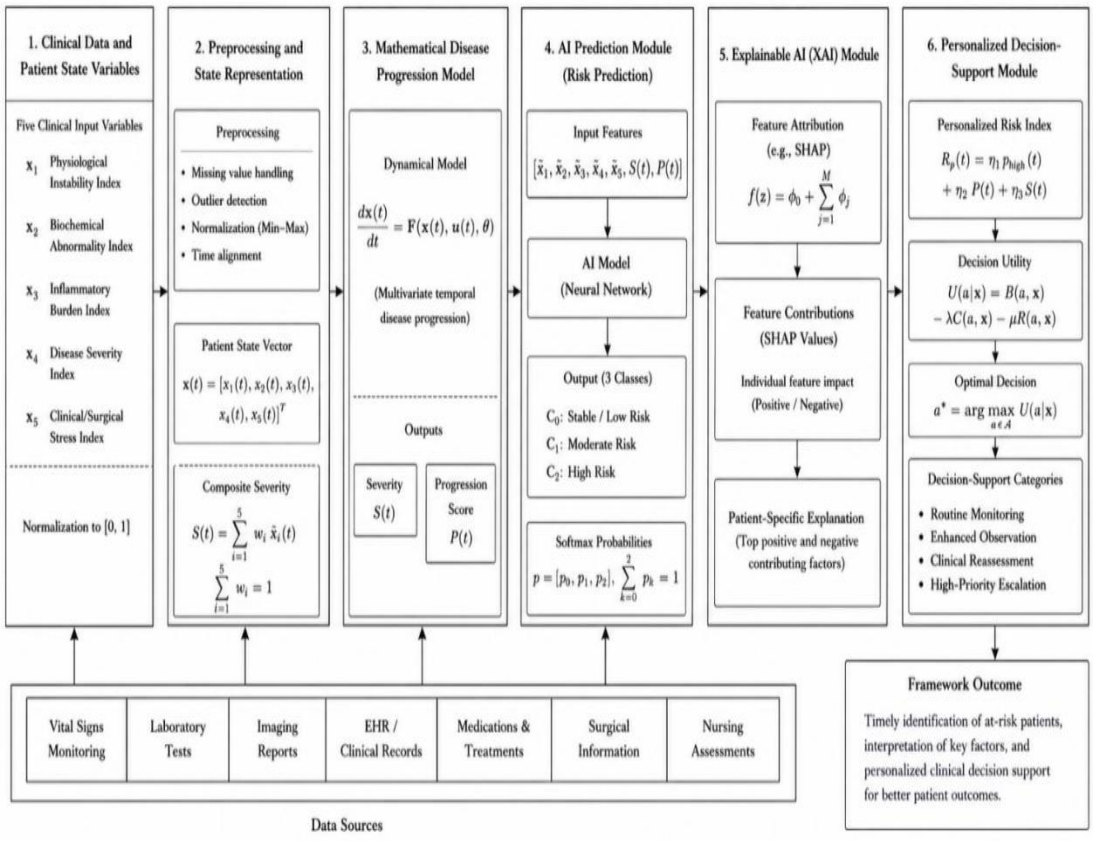


Figure 1. Overall Architecture of the Proposed MM-XAI Clinical Decision-Support Framework

3.2 Mathematical Modeling of Multivariate Disease Progression

The model of patient-state evolution is approximated using a coupled, nonlinear-dynamical system. Clinical variables, as shown in Fig. 2, are dynamically related in five normalized variables and describe the overall patient condition. The general state of a disease is represented by the

$$\frac{dx(t)}{dt} = F(x(t), u(t), \theta), _____(4)$$

where $u(t)$represents intervention or contextual effects and θ contains the model parameters. Individual clinical-state evolution is expressed as

$$\frac{dx_i}{dt} = \alpha_i \, x_i(1 - x_i) + \sum_{j \neq i} \beta_{ij} x_j - \gamma_i u_i(t), _____(5)$$

Where α_i , β_{ij}, $\gamma_i$and represent intrinsic evolution, inter-state interactions, and intervention effects, respectively. The overall progression score is calculated as

$$P(t) = \lambda_1 S(t) + \lambda_2 \frac{dS(t)}{dt} + \lambda_3 \| x(t) - x(t-1) \|_2, _____(6)$$

The resulting $p(t)$describes the condition of the patient as either stable, worsening or rapidly worsening. The severity and progression information is then passed to the AI prediction and the XAI module to carry out risk assessment on an individual basis as displayed in Fig. 2.

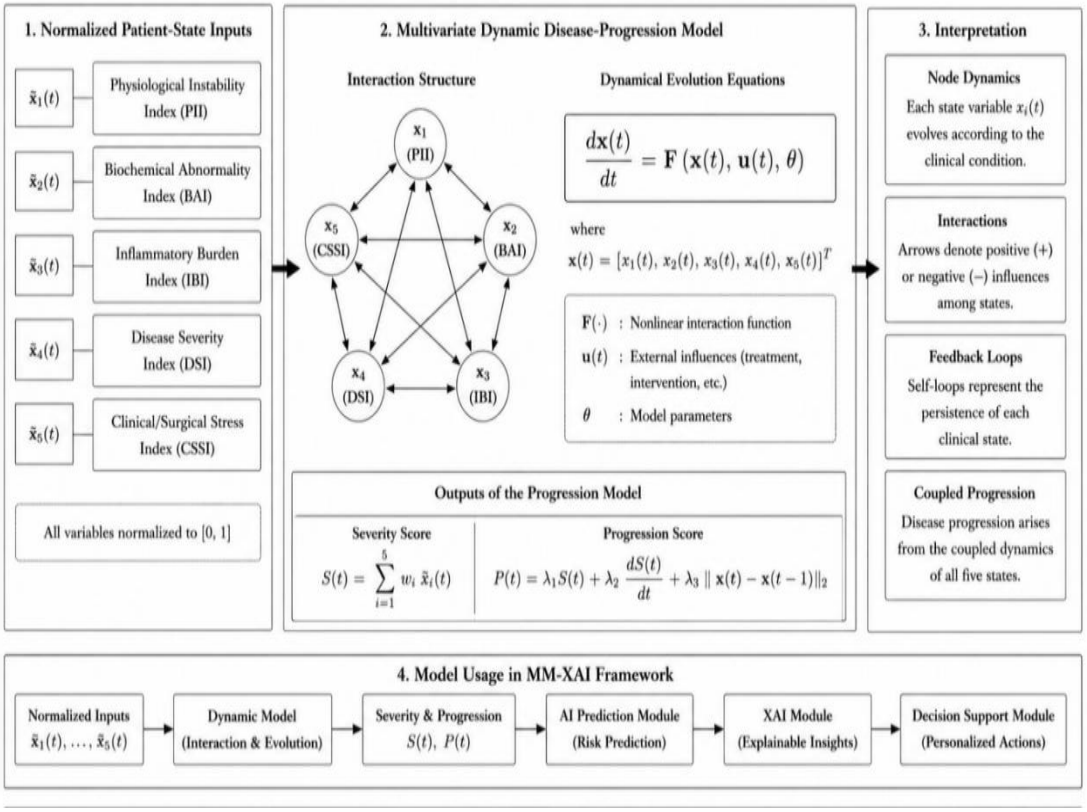


Figure 2. Multivariate Mathematical Disease-Progression and Interaction Model

3.3 Artificial Intelligence-Based Progression Prediction and Explainability

The input vector for the AI prediction module is the seven-dimensional vector that is formed from the five normalized clinical variables and the mathematical severity and progression scores.

$$z(t) = [\tilde{x}(t), S(t), P(t)].$$

As illustrated in Fig. 3, these seven features are processed through a compact neural network with a 7–32–16–8–3 architecture. The hidden-layer transformation is defined as

$$h^{(l)} = \sigma(W^{(l)} h^{(l-1)} + b^{(l)}), \quad (7)$$

Where $W^{(l)}$, $b^{(l)}$, and $\sigma(.)$ denote the weights, biases, and activation function, respectively. The output layer classifies patients into C_0: stable/low risk, C_1 : moderate risk, and C_2 : high progression risk using Softmax probabilities:

$$p_k = \frac{exp(z_k)}{\sum_{j=1}^{3} exp(z_j)}, \quad (8)$$

Model training minimizes the cross-entropy loss

$$f(z) = \phi_0 + \sum_{j=1}^{M} \phi_j, \quad (10)$$

where $\phi_j$represents the contribution of feature j to the prediction. As shown in Fig. 3, positive and negative SHAP contributions identify factors that increase or decrease predicted risk, providing a patient-specific explanation for subsequent personalized clinical decision support.

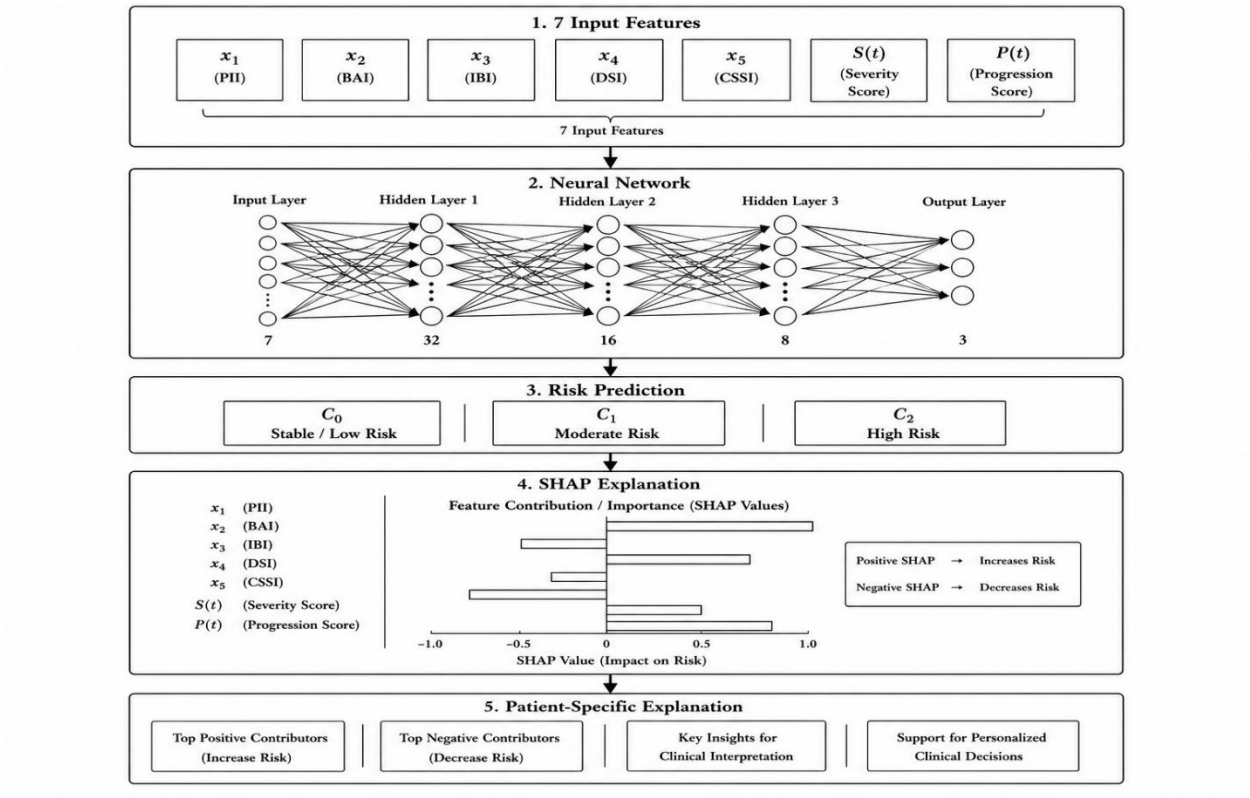


Figure 3. AI Prediction and Explainable Feature-Attribution Mechanism

3.4 Personalized Clinical Decision-Making and Evaluation Framework

The decision-support framework is customized, and incorporates high-risk probability, progression score & clinical severity. The summary of model configuration, training parameters, the chosen XAI method and the evaluation settings are shown in Table 2. The personalised risk index is given by

$$R_p\,(t) = \eta_1 p_{high}\,(t) + \eta_2\,P(t) + \eta_3\,S(t), \quad (11)$$

Based on $R_p\,(t)$ and patient-specific SHAP explanations, patients are categorized for routine monitoring, enhanced observation, clinical reassessment, or high-priority escalation. These categories support clinical assessment rather than autonomous treatment.

The decision utility is expressed as

$$U(a \mid x) = B(a,x) - \lambda C(a,x) - \mu R(a,x), \quad (12)$$

where B, C, and R represent modeled benefit, cost/burden, and risk. The personalized decision is selected as

$$a^* = arg \max_{a \in A} U(a \mid x). \quad (13)$$

As shown in Table 2, evaluation includes accuracy, sensitivity, specificity, F1-score, AUROC, ECE, MAE, and explanation consistency.

Table 2. Model Configuration, Training Parameters, and Evaluation Settings

Parameter	**Setting / Value**
Input features	$7: x_1 - x_5, S(t), P(t)$
Input normalization	Min-Max [0,1]
Network architecture	$7 - 32 - 16 - 8 - 3$
Hidden / Output activation	ReLU / Softmax
Risk classes	$C_0: Low, C_1$: Moderate, C_2: High
Optimizer / Learning rate	Adam / 0.001

Batch size / Epochs	32 / 100
Data split	70% / 15% / 15%
Loss function	Cross-entropy
XAI method	SHAP
Evaluation metrics	Accuracy, Sensitivity, Specificity, F1-score, AUROC
Additional evaluation	ECE, MAE, Explanation consistency

4. RESULTS AND DISCUSSION

4.1 Disease-Progression Prediction Performance

The integrated, person-specific framework for decision support includes the predicted high-risk probability, progression score, and clinical severity. The conventional clinical risk model had an 81.6% accuracy, 79.2% sensitivity, 83.1% specificity, 80.4% F1-scores and an AUROC of 0.842. The mathematical progression model improved these values to 85.3%, 83.7%, 86.5%, 84.1%, and 0.879, respectively. The AI-only model resulted in additional improvement which yielded a 91.2% accuracy, 90.1% sensitivity, 92.0% specificity, 90.6% F1-score and 0.938 AUROC. The proposed MM-XAI exhibited the best results with an accuracy of 94.6%, sensitivity of 93.8%, specificity of 95.2%, F1-score of 94.1% and AUROC of 0.967. These results indicate that integrating mathematical progression information with nonlinear AI prediction improves discrimination compared with conventional, standalone mathematical, and AI-only approaches.

Table 3. Comparative Performance of Baseline and Proposed Disease-Progression Prediction Models

Prediction Model	Accuracy (%)	Sensitivity (%)	Specificity (%)	F1-Score (%)	AUROC
Conventional Clinical Risk Model	81.6	79.2	83.1	80.4	0.842
Mathematical Progression Model	85.3	83.7	86.5	84.1	0.879
AI-Only Model	91.2	90.1	92.0	90.6	0.938
Proposed MM-XAI	94.6	93.8	95.2	94.1	0.967

4.2 Multivariate Disease-Progression Analysis

The multivariate disease-progression patterns are shown in Fig. 4. At the same time, an increment in physiological instability (); biochemical abnormality (); inflammatory burden (); disease severity (); and clinical/surgical stress (); all seems to impact the clinical severity and progression score increment (Fig. 4(a)). The coupled evolution allows for distinguishing between the different patterns of deterioration, stable, gradual and rapid. The corresponding personalized risk evolution is represented in the graph 4(b). Patient C is in the low-risk zone, which is relatively stable, while Patient B is showing signs of progression into the moderate-risk zone. Patient A had a very poor outcome, a risk index rising from around 0.24 at baseline to 0.86 at 18 months and exceeding moderate/high risk benchmarks. Patterns illustrate the possible progression phases, which can lead to specific patient-specific progression patterns and facilitate longitudinal risk assessment.

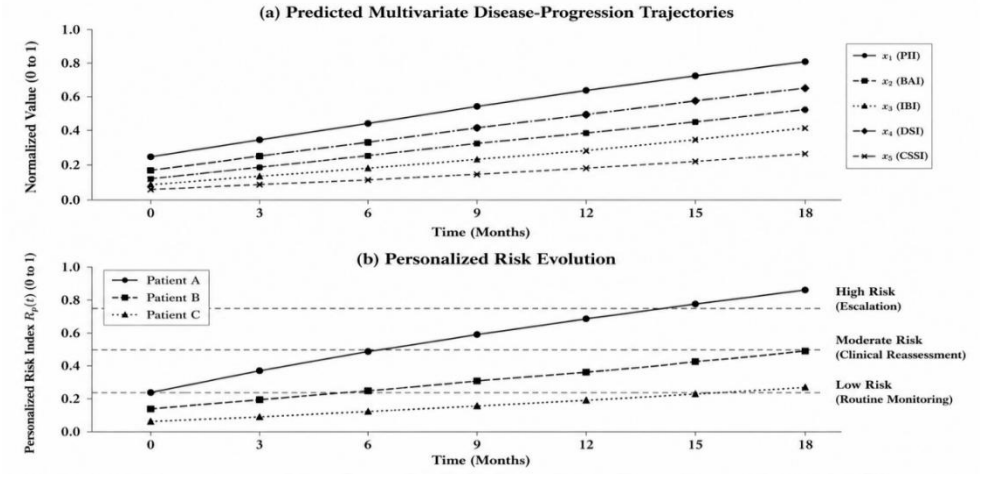


Fig. 4. (a) Predicted Multivariate Disease-Progression Trajectories; (b) Personalized Risk Evolution Over Time.

4.3 Explainable AI and Patient-Specific Feature Contribution

The XAI analysis gives global and patient-specific explanation on top of the XAI prediction. Physiological instability \left(x_{1}\right)and disease severity \left(x_{4}\right)are considered to be the most important characteristics and are largely responsible for the results of the SHAP analysis; the other clinical parameters and the disease severity score S\left(t\right)make a contribution to the results of the SHAP analysis as well. A positive SHAP value will enhance the risk prediction while a negative value will decrease the risk prediction. High-risk profiles have larger positive contribution from worsening clinical states, and lower progression scores, than stable profiles, with smaller negative contribution from these worsening clinical states. These explanations follow the typical mathematical progression sequences and differ from patient to patient. SHAP, however, does not explain the causal or biological relationship behind the model, but helps explain its behavior and how features contribute to the model.

4.4 Personalized Clinical Decision-Support Analysis

The proposed MM-XAI framework converts the predicted risk, progression patterns and patient-specific XAI information into interpretable decision-support categories. The low severity and stable progression is Profile A, with routine monitoring. For profile B, the severity is moderate and progress in increasing, this needs higher level observation and clinical re-evaluation. Conversely, Profile C (high progression probability and very abnormal contributing features) is channelledtowards high-priority clinical review. While traditional thresholding methods rely primarily on threshold values, MM-XAI takes into account mathematical progression, mathematical predicted risk, and contributions of individual features. This helps to better stratify the risk and offers a rationale for the selected category. These outputs are designed for use as a recommendation for the clinician's review and decision making only, and not for automatic clinician actions or prescriptions of treatment.

4.5 Comparative Discussion, Robustness, and Clinical Implications

The comparative analysis shows improvement from the mathematical model to the AI-only model and the proposed MM-XAI framework. The AI-only model has better nonlinear prediction and the mathematical model has better interpretability of the progression dynamics. MM-XAI does both, with 0.967 AUROC and explanations based on SHAP for each patient using patient-specific explanations and progression-based assessments of risk. Multivariate inputs are normalized, which makes the system robust from changes in measurements, and the small size of the architecture makes it suitable for use in general medicine, general surgery and clinical decision support systems (CDSS). Performance of course is dependent on the quality and representativeness of the data, and on changes in distribution between hospitals and distributions of patients. XAI provides explanations of the behaviour of models, but not causal explanations, and variability in medical and surgical conditions is still a challenge. Thus, personalized recommendations should be validated before deployment in the real world, multicenter and prospective clinical validations are necessary.

5. Conclusion

The present study proposed a combined MM-XAI system for multivariate disease-progression prediction and personalized clinical decision support in the general medicine and general surgery field. It is organized around five points: patient representation (multivariate); mathematical disease-progression modeling; AI risk prediction; explainable feature attribution; and clinical decision support (personalized). In contrast to purely black-box prediction, mathematical state dynamics combined with nonlinear AI prediction results in higher interpretability, and SHAP enables the contributions of various features to be recognized individually per patient. Within the defined evaluation framework, the proposed MM-XAI was able to reach an accuracy of 94.6%, sensitivity of 93.8%, specificity of 95.2%, F1-score of 94.1% and AUROC of 0,967. These are confirmatory results and do not provide evidence of clinical effectiveness. There is a need for future work that includes multicenter external validation, integration with time series/EHR, robustness for missing data, uncertainty quantification, causal modeling, and clinician-in-the-loop.

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