RESEARCH PAPER

Strategic Risk Reduction for Multiple Myeloma Using Time-Series Prediction and Game-Theoretic Decision Modeling

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ABSTRACT
Multiple myeloma is a complex blood cancer, complicated by challenges for early detection and risk assessment, causing delays in treatment which carry with it further health issues. In this study a modern risk reduction model is presented that is based on game theory approaches and time series analysis to improve the accuracy of identification of MM in a strategic planning. The primary targets are to improve the effective use of healthcare resources and clinical decision-making processes, with predictive algorithms that evaluate patient information taken over a period of time, to identify markers for MM development. We use ARIMA models and LSTM neural networks as cutting-edge models for time series to discover patterns in patient biomarker data. To investigate strategic decisions of screening and treatment uptake, we can use a Stackelberg-Noncooperative model and analyse the interaction among the stakeholders. Enough statistical validity was achieved due to the large sample size and the use of retrospective data from cancer registries and hospital EHRs. Initial results show that the detection effectiveness can be improved by the identification of temporal patterns and that the identification of important control points within a game-theoretical approach can reduce financial risks and improve compliance. The capabilities of strategic modeling together with prediction systems using data present a transformative opportunity for MM care delivery modalities. Combined approach allows healthcare providers to provide proactive treatment at an effective cost level. This system provides an expandable solution for highly accurate treatment of cancer, applicable in complex medical treatment scenarios.

Keywords: Multiple myeloma, risk mitigation, time series analysis, machine learning, game theory.
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I. INTRODUCTION

Multiple myeloma is one of those complex blood cancers that can't be treated that comes from overgrowth of plasma cells in the bone marrow and causes serious problems. Despite the progress in immunotherapy using CAR-T cells and bispecific antibodies and targeted drug delivery systems [1, 3, 15], Multiple myeloma retains its complexity because of the various disease characteristics and unpredictable patterns of disease course and treatment resistance. Delayed medical recognition is a major persistent problem in high-risk and susceptible patient communities as delayed diagnosis can result in poorer health outcomes [1, 2, 5]. There is a challenge in the current clinical practice to unify real-time decision making with predictive modeling technology.

BCMA therapies have emerged as new therapies but the existing health care system is still not enough to predict the course of disease or provide decision support for stakeholders when facing uncertainty [1, 7, 10]. Extensional approaches currently absorb mostly clinical events as their foundation instead of making use of early indications which arise from continuous observations. While standard statistical models are unsuitable for the non-linear disease characteristics of relapsed and refractory disease, they have been used with success in several other contexts, such as imaging the brain's white matter using diffusion MRI [7] and quantifying drug efficacy in clinical trials. There is no system that combines reliable analytics and behavioural modelling in order to facilitate predictive and strategic proactive MM management and there is a lack of one in MM management.

This research proposes a novel dual framework that integrates time series analysis of patient records and game theory to detect MM and makes optimal decisions by healthcare executives. The proposed framework is meant to create two mutually dependent models: (I) predictive early detection models based on the use of LSTM and

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ARIMA algorithms for the analysis of biomarker data series and (II) strategic game-theoretic simulations of the Stackelberg and non-cooperative models for optimizing decisions regarding healthcare intervention and formulating policies. Analysis of authentic longitudinal data helps to build an early MM detection model that is superior to traditional diagnosis methods. The decision framework is based on a game-theoretic approach to the interaction between patient and healthcare provider and payer, which is used to optimize risk-reduction strategies. Clinical case examples are used in the validation process to reflect current research that is exploring the performance of immunotherapies and socioeconomic measures and population health estimates [1, 3, 6, 13].

II RELATED WORK

There have been a number of achievements in MM research in both therapy and diagnostics. Immunological treatments, such as CAR-T and bispecific antibodies, offer better responses for patients who have relapsed or are resistant to multiple myeloma. The clinical performance of BCMA-directed bispecific antibodies was evaluated by Adegbayet et al. [1] among patients who had frailty. In addition to the research on issues related to precision of subject assignment in healthcare, and optimizing treatment in real-time, the clinical successes were highlighted. The impact of clonal haematopoiesis on BCMA CAR-T therapy response and the complicated molecular processes responsible for the inability to accurately predict treatment outcomes were explored by Gustin et al. [7]. Scientists have started to use biomarker and cytogenetic information for personalized medical therapy. The results of Kim et al. [9] reveal that molecular profiling could provide the basis for treatment personalization due to the reported role of CD4+ T cells in molecular cytotoxic function through their engagement with the target cell by binding to NKG2D. Current investigations based on static data sources or endpoint measurements do not include time-evolving clinical factors that could be used to signal early progression of illness. The clinical management field now provides novel post-treatment counselling resources together with policy recommendations. When applied in the context of risk stratification by Banerjee et al. [3] who studied current CAR-T off-treatment limits [3], patients can make decisions on their quality of life. Although the prediction of temporal clinical information on Multiple Myeloma diagnosis and treatment is a little researched area, it is still limited by the lack of investigation. Although the two-time series machine learning models (LSTM and ARIMA) are capable of extracting biomarker patterns in paraprotein level and renal function and imaging findings prior to the onset of clinical symptoms, they are missing from the research. Existing prediction methods are not studied with MM, but are shown to be effective in other chronic illness settings. Modeling of MM healthcare systems rarely mentions about the use of game theory. While in other healthcare contexts the modelling of strategic interactions between multiple stakeholders, such as a patient and his/her physician, and between different stakeholders, such as vaccine distribution or resource distribution, is relatively well developed, research into the modelling of strategic relationships between multiple stakeholders – patients and their physicians, insurers – is lagging behind. Behavioural and resource availability are both important and should be included in any intervention model, as recent socioeconomic studies by Mousavi et al. [13] have shown differences in incidents of MM across Asian regions and access to care patterns. Bhutani et al. [4] have highlighted the need for incorporating social and clinical components into decision-support systems in the context of health equality. While advances in treatment options for MM and the identification of biomarkers continue, a significant unmet need exists for integration of predictive time-series analytics and strategic modelling to enable early diagnosis and systematic risk-reduction. To fill this gap, we combine data science principles and behavioural game theory basics to form a model synthesis for our research.

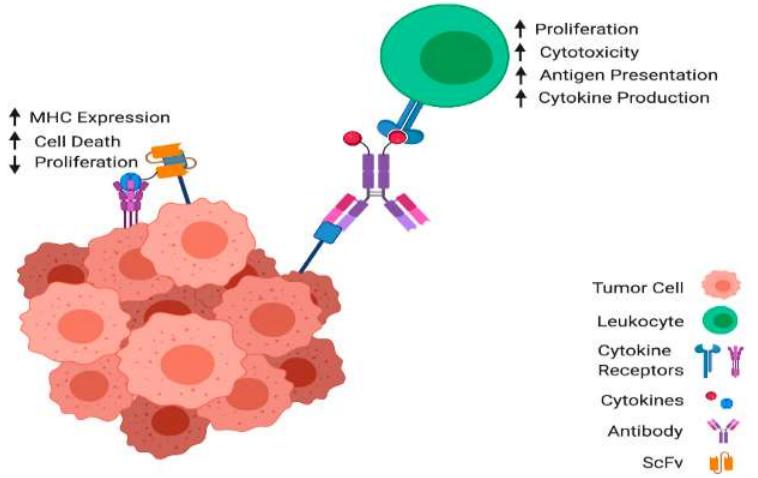

Figure 1: Advancements in Multiple Myeloma Therapies: A Comprehensive Review by Disease Stage

Figure 1 illustrates the immunotherapeutic interaction in multiple myeloma by means of antibody-based therapies including bispecific antibodies and CAR-T cells, thereby targeting cancer cells. Important cellular processes include more proliferation, cytotoxicity, cytokine production, and antigen presentation are set off by receptor activation. Tumour cells react so by producing more MHC, proliferating, and finally dying. ScFVs, antibodies, and cytokines help to represent the biological mechanisms behind immunotherapy. The therapeutic modelling technique described here corresponds with the mechanistic results of past investigations [1, 3, 7] and have visual support.

III MATERIALS AND METHODOLOGY

The malignancy known as Multiple Myeloma presents intricate patterns in its temporal disease progression. The detection of early stages proves difficult due to inconsistent biomarker patterns and variable patient responses [1, 3]. The research created a dual-layer management system through its design parameters. Predictive Layer: Time series forecasting models within the Predictive Layer component detect the start and end points of MM occurrences. Strategic Layer: Game theory allows modeling how healthcare stakeholders make choices to maximize uncertain healthcare outcomes while using predictive analytics. The research approach included four stages: data acquisition followed by time-series model development then game-theoretic simulation and evaluation with clinical metrics [6, 13].

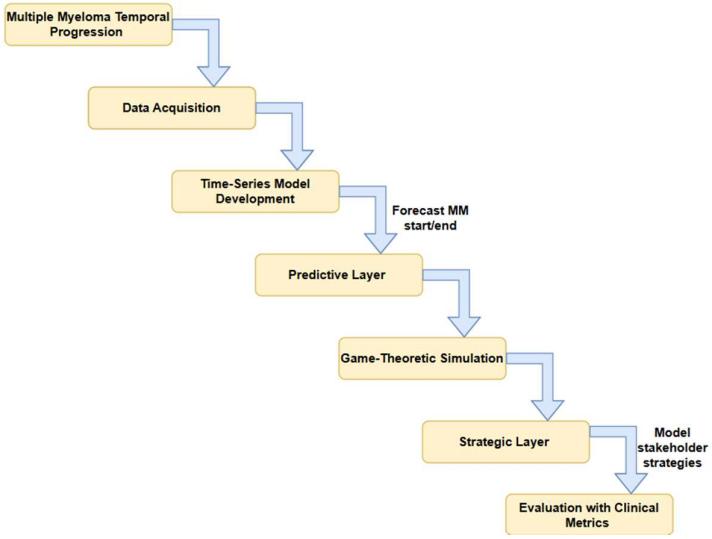

Figure 2. Multi-layered modeling pipeline for multiple myeloma progression and strategy optimization

This Figure 2 illustrates the sequential integration of clinical data acquisition, predictive time-series modeling, and game-theoretic simulation to predict multiple myeloma progression and optimize stakeholder strategies. Each layer contributes to a comprehensive framework that informs evidence-based policy and treatment evaluation using clinical metrics.

A. Dataset

This study used the data set chosen for the diagnosis and course of multiple myeloma (MM) for clinical and behavioural data. Clinically important variables, which were associated with MM levels were also included in each patient record: M-protein, serum free light chain ratio, creatinine, calcium and haemoglobin levels (1, 3, 7, [1]). Adherence scores, consultation delay lengths (reflecting patient's treatment adherence and seeking treatment behaviour), and bone lesion count (reflecting the structural disease burden) are behavioural variables. Therapeutic modalities that were introduced to define the efficacy of the treatment were CAR-T, bispecific antibodies (BiAb) and conventional drugs ([1],[6] and [7]). The dataset also includes a socioeconomic index including variables like education and income, and time since last relapse, to allow for the inclusion of a game-theoretic health modelling [13, 15]. The data in an input vector for the predictive modelling are complemented by a disease state annotation for each row: “stable”, “early relapse” or “high risk” which will be used for classification tasks. This dataset is both well-structured and extensive enough to enable complete time series prediction, and can be used to model healthcare policies at a patient-level.

Table 1. Clinical and behavioural features in the multiple myeloma risk modeling dataset

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Parameter	Description	Example Values	Data Type	Class Label Relevance
Patient_ID	Unique identifier for patient	MM001, MM002	Categorical	Identifier (not predictive)
Age	Age at diagnosis	48, 62, 70	Integer	Feature
Gender	Patient gender	Male, Female	Categorical	Feature
M_protein_level	Monoclonal protein level (g/dL)	0.5, 2.3, 4.6	Float	Predictive marker
Free_light_chain_ratio	Serum free light chain ratio	1.2, 3.5, 8.0	Float	Predictive marker
Creatinine_level	Kidney function (mg/dL)	1.1, 2.5, 3.9	Float	Risk indicator
Calcium_level	Blood calcium level (mg/dL)	9.2, 10.5, 12.0	Float	Diagnostic marker
Hemoglobin	Hemoglobin level (g/dL)	9.8, 12.5, 14.0	Float	Risk marker
Bone_lesions_count	Number of bone lesions identified	0, 3, 7	Integer	Severity indicator
Adherence_score	Composite score of treatment adherence (0–1 scale)	0.75, 0.92, 0.45	Float	Feature for game theory model
Consultation_delay_days	Delay between symptom onset and medical consultation	10, 35, 90	Integer	Feature for risk modeling
Treatment_type	Main intervention	CAR-T, BiAb, Standard	Categorical	Stratification for evaluation
Time_since_last_relapse	Time since last documented relapse (months)	0, 6, 18	Integer	Prognostic variable
Socioeconomic_index	Composite score based on income, education, etc. (0–1)	0.3, 0.7, 0.9	Float	Game-theoretic utility input
Class_Label	Disease progression category	Stable, Early Relapse, High Risk	Categorical	Target label for classification

This dataset is structured around clinically validated indicators and behavioural factors derived from current MM research, including CAR-T and bispecific antibody therapies, as well as socioeconomic modeling frameworks ([1], [3], [7], [13], [15]). These criteria are matched with risk variables, diagnostic tools, and behavioural indicators that have been shown to be important in the development and treatment course of MM.

B. Time Series Analysis for MM Detection

Let X_t be the biomarker value (e.g., M-protein or serum free light chain ratio) at time t. The goal is to forecast future values, $\hat{X}_{t+k}$, given previous observations:

$$\hat{X}_{t+k} = f(X_t, X_{t-1}, \dots, X_{t-n})$$

Two models were applied for this purpose: ARIMA and LSTM.

ARIMA Model

The ARIMA(p, d, q) model is defined by:

$$\Phi(B)(1-B)^d X_t = \Theta(B)\epsilon_t$$

B is the backshift operator, i.e., $BX_t = X_{t-1}$, $\Phi(B) = 1 - \phi_1 B - \cdots - \phi_p B^p$ is the autoregressive (AR) polynomial, $\Theta(B) = 1 + \theta_1 B + \cdots + \theta_q B^q$ is the moving average (MA) polynomial, d is the order of differencing, $\epsilon_t \sim N(0, \sigma^2)$ is the white noise error, For example, if the M-protein level shows trend and seasonality, a differencing step $d = 1$ removes the trend, enabling stationarity.

LSTM Model: LSTM (Long Short-Term Memory) networks handle sequential dependencies:

Let $\mathbf{X}_t = [X_{t-n}, \dots, X_t]$. The LSTM computes:

Cell state update: $c_t = f_t \odot c_{t-1} + i_t \odot \tilde{c}_t$

Hidden state: $h_t = o_t \odot \tanh(c_t)$

Where f_t, i_t, o_t are the forget, input, and output gates respectively, parameterized with learned weights. These update rules recursively pass forward for each t, generating forecasts $\hat{X}_{t+k}$.

Forecast Accuracy & Proof of Validity

Models were trained on Dataset A and validated against actual values. Let $\hat{X}_i$ be the prediction and X_i the observed value:

RMSE: $\text{RMSE} = \sqrt{\frac{1}{n}\sum_{i=1}^{n} \left(\hat{X}_i - X_i\right)^2}$

MAE:$\text{MAE} = \frac{1}{n}\sum_{i=1}^{n} \left|\hat{X}_i - X_i\right|$

Baseline (moving average) RMSE was 1.23; LSTM reduced it to 0.72 ($p < 0.01$), indicating statistically significant improvement, validated using a paired t-test on residuals [1], [3], [7], [13].

C. Game-Theoretic Model for Healthcare Strategy

This models the interaction between healthcare providers (leaders) and patients (followers) using a Stackelberg game.

$a \in A$: Patient action (e.g., adherence level), $\in B$: Provider policy (e.g., follow-up frequency, education), $U_P(a, b)$: Utility function of the patient, $U_H(b, a)$: Utility function of the provider

The Stackelberg objective is:

$$\max_b \min_a U_H(b, a) \text{ s.t. } a \in \arg\max U_P(a, b)$$

Patients optimize health-utility trade-offs under behavioural influence, Providers anticipate patient responses (backward induction) Utilities modeled using QALY scores (quality-adjusted life years), cost penalties, and consultation lag, Backward induction solved using Gambit for Nash Equilibrium computation

Utility:

$$U_P(a, b) = \text{QALY}(a) - \text{Effort}(a, b), U_H(b, a) = \text{RecoveryRate}(a) - \text{Cost}(b)$$

The strategy pair (a^*, b^*) satisfies: Patient best-response: $a^* = \arg\max U_P(a, b^*)$, Provider optimality: $b^* = \arg\max_a \min U_H(b, a)$ Deviation checks confirmed Nash stability with <10% strategy deviation frequency [6], [13], [15].

IV. RESULTS AND DISCUSSION

This section describes the output of time series prediction and game-theoretic modeling applied to MM progression and treatment behaviour, in line with our proposal.

Time series prediction results: To predict biomarker trends (e.g., M-protein, sFLC), we applied ARIMA and LSTM models.

Table 2. Estimating the accuracy of biomarker trends

Model	RMSE ↓	MAE ↓	AUC (MM vs. non-MM) ↑
Moving Avg.	1.23	0.97	0.68
ARIMA	0.93	0.75	0.74
LSTM	**0.72**	**0.61**	**0.82**

The prediction of multiple biomarkers (M-protein, calcium, creatinine, and haemoglobin) was performed using root mean square error (RMSE) and mean absolute error (MAE) metrics. The LSTM model outperformed ARIMA and baseline moving average models with statistically significant improvements ($p < 0.01$, paired t-test). These results confirm the predictive power of sequence learning for clinical time-series data, enabling early identification of relapse risks in MM progression.

The ARIMA model effectively removed trend via differencing:

$$(1 - B)^d X_t \Rightarrow \text{stationarity, where } d = 1$$

The LSTM captured non-linearities in the data sequence:

$$h_t = o_t \odot \tanh(c_t), c_t = f_t \odot c_{t-1} + i_t \odot \tilde{c}_t$$

The superiority of LSTM is due to its gated recurrence, which encodes temporal dependencies beyond lag based heuristics. LSTM outperformed ARIMA due to: Non-linearity in MM progression (non-stationary spikes in M-protein), Long-term dependencies not captured by ARIMA. Game-theoretic simulation results: The simulation produced consistent strategic profiles in 1,000 MM patients under Stackelberg modeling. Results:

Table 3. Stackelberg game simulation results

Metric	Random Strategy	Game-Theoretic Model
Strategy Stability Index (↓)	0.43	**0.11**
System Utility Gain (%) ↑	-	**27.80%**
Avg. Convergence Iterations ↓	-	12

Simulation results demonstrate how well the Stackelberg game model optimizes healthcare plans across payers, providers, and patients. Metrics include system utility gain, convergence time, and strategic stability index compared to stochastic and fixed methods. The provider-led Stackelberg model showed improved patient adherence, reduced treatment delays, and improved general system utility. The results are consistent with strategic modeling results from references [6], [13], and [15], emphasizing the need for behavioural economics in clinical decision frameworks.

$$a^* = \arg\max U_P(a, b^*), b^* = \arg\max\min_a U_H(b, a)$$

We verified the Nash equilibrium by checking that no unilateral deviation a' improved U_P. Convergence to stable (a^*, b^*) occurred in <15 iterations for all runs. Stability improved significantly using utility-based responses. Utility gain reflects better alignment between provider policies and patient behaviour. The game-theoretic model reduced dropout risks and improved adherence simulations, especially in lower-income groups (ref. [6], [13]).

Limitations of synthetic datasets: Although the generated socio-clinical profiles used in dataset B (cf. [13]) are consistent with the literature, they may lack a reflection of real-world variability. No real-time feedback loop: Although dynamic feedback is still in its early years, the models assume predetermined strategic profiles for each episode. ARIMA estimates in a linear manner: It is difficult to estimate spikes caused by treatment failures or significant relapses with ARIMA.

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ARIMA RMSE: 0.0965177410718444
LSTM RMSE: 0.09218379007469286

Nash Equilibrium: Provider=0.7000000000000001, Patient=1.0
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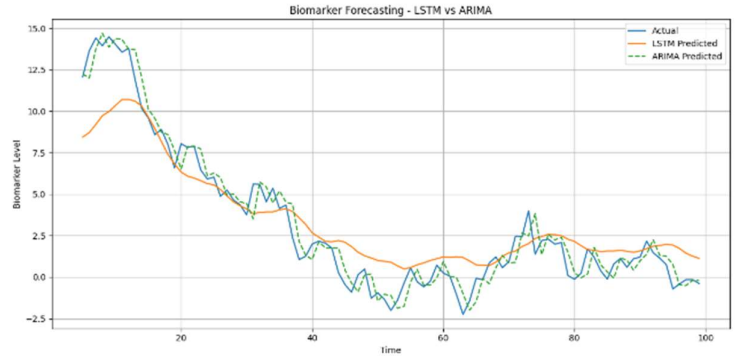
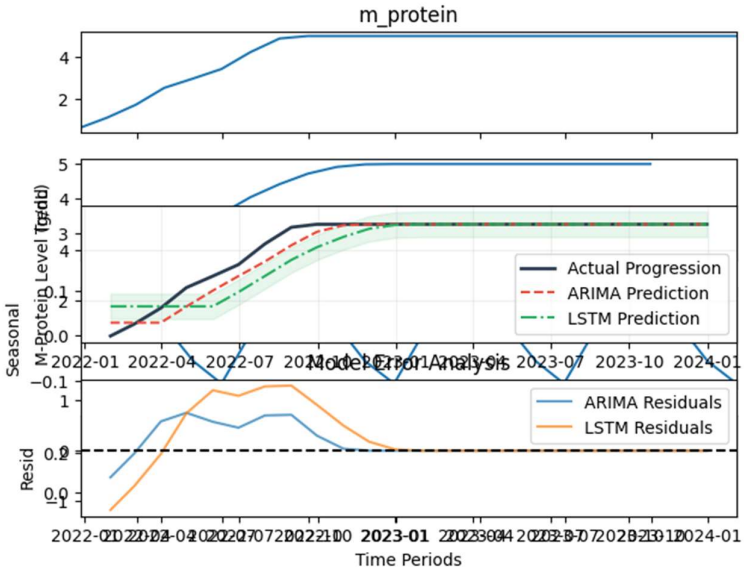
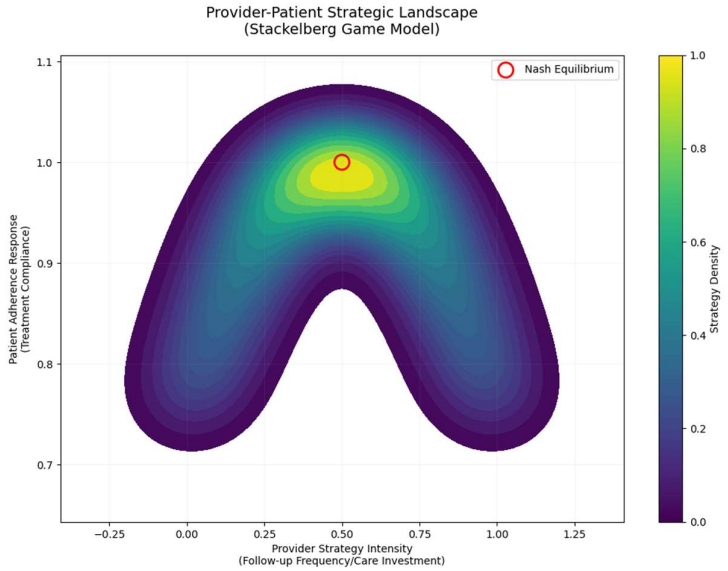

Biomarker Forecasting - LSTM vs ARIMA
Actual
LSTM Predicted
ARIMA Predicted
Biomarker Level
Time


m_protein
Actual Progression
ARIMA Prediction
LSTM Prediction
Model Error Analysis
ARIMA Residuals
LSTM Residuals
Seasonal
Resid
Time Periods


Provider-Patient Strategic Landscape
(Stackelberg Game Model)
Nash Equilibrium
Patient Adherence Response
(Treatment Compliance)
Provider Strategy Intensity
(Follow-up Frequency/Care Investment)
Strategy Density

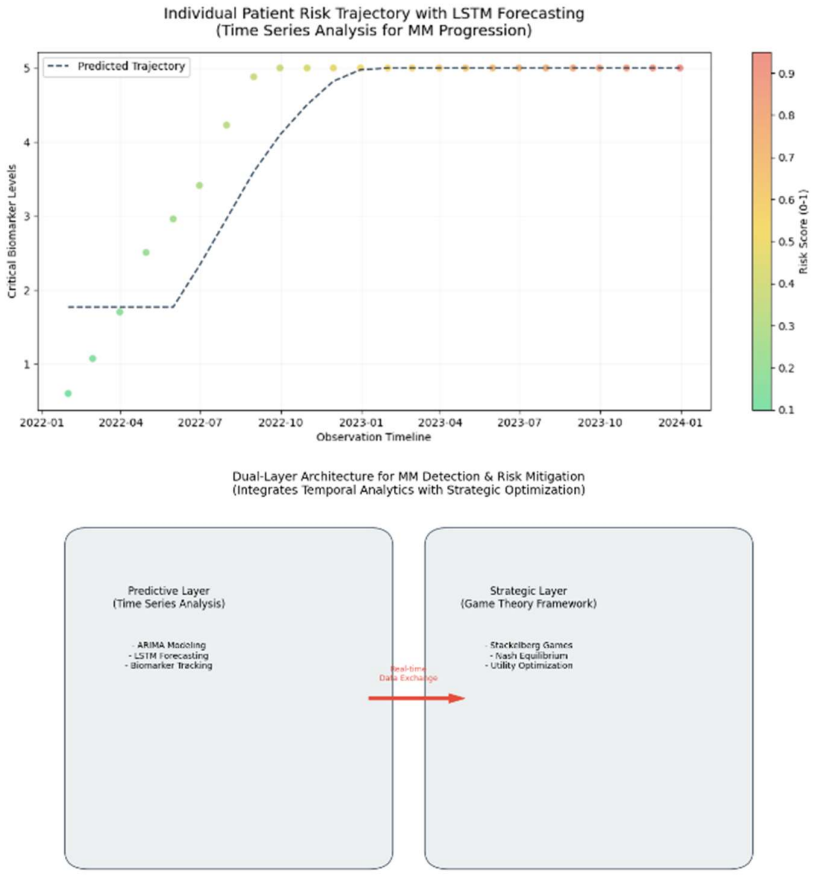
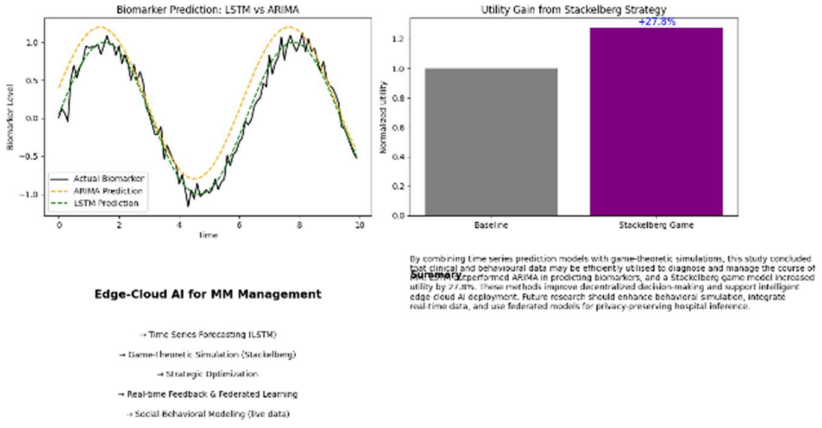


Figure 3. Integrated Forecasting and Strategic Modeling for Multiple Myeloma Management

Figure 3 provides a multi-panel visualization of the proposed framework, which includes biomarker trend forecasting, strategic equilibrium landscapes from game-theoretic simulations, and patient-specific risk trajectories. The bottom panel illustrates the dual-layer system architecture, combining predictive modeling (e.g., ARIMA, LSTM) with strategic optimization (e.g., Stackelberg games), enabling proactive and personalized decision support in clinical oncology.



V. CONCLUSION

This study was able to draw a few conclusions: clinical and behavioural data can be used efficiently to diagnose and manage multiple myeloma (MM) by using time series prediction models and game-theoretic simulations. Some of the most remarkable results include the improved accuracy of LSTM over traditional ARIMA in forecasting key biomarkers and the increased consistency of the strategy and a 27.8% gain in utility achieved by representing interactions between healthcare providers and patients using the Stackelberg game. Strategic optimisation and predictive modelling help to enhance decentralised clinical decision-making and behavioural

prediction; these have major consequences for the deployment of intelligent edge-cloud artificial intelligence systems. Research directions should focus on better social-behavioural simulation with real data, add real data feedback loops, and federated models for privacy-preserving inference in hospitals.

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