TAPS-AD: A Transparent Multi-Agent Large Language Model Framework for Personalized Alzheimer's Disease Prognosis and Evidence-Based Intervention

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***Abstract*—Alzheimer's Disease (AD) diagnosis models predominantly focus on binary risk classification, lacking the ability to predict the rate of cognitive decline and provide interpretable clinical decisions. We propose TAPS-AD (Transparent Multi-Agent Prognostic and Intervention System for AD), a novel multi-agent framework leveraging specialized Large Language Model (LLM) agents that analyze heterogeneous patient data: longitudinal electronic health record (EHR) clinical notes, structured biomarker data, and connected speech features. Coordinated by a central Orchestrator, TAPS-AD produces individualized quantitative predictions of the annual Mini-Mental State Examination (MMSE) decline rate, alongside personalized, evidence-based lifestyle and clinical trial interventions. Crucially, the system integrates a transparency pipeline where each agent presents its top influential features with confidence scores, enabling conflict resolution and generating an auditable, explanatory rationale that enhances trust and clinical utility. TAPS-AD advances AD care through dynamic prognosis and actionable insights, bridging the gap between state-of-the-art artificial intelligence and practical clinical decision-making.**

I. INTRODUCTION

Alzheimer's Disease (AD) is a progressively debilitating neurodegenerative disorder characterized by cognitive decline with profound health and socioeconomic impact worldwide. Early diagnosis and personalized management are imperative to maximize therapeutic effects and optimize patient quality of life. While recent advances in artificial intelligence, specifically large language models (LLMs), have demonstrated promise in AD risk classification from single modality data sources, these approaches often fall short in capturing the dynamic nature of cognitive decline trajectories or generating transparent, clinically interpretable outputs. Current state-of-the-art models primarily offer binary or multiclass classification (e.g., healthy, mild cognitive impairment, AD), limiting their applicability in individualized prognosis and treatment planning. Furthermore, the "black-box" nature of these models hampers clinical trust, assessment, and adoption. To address these critical gaps, we introduce TAPS-AD, a transparent multi-agent LLM framework designed to: Predict the annual rate of MMSE score decline, a clinically relevant quantitative measure of cognitive deterioration, using longitudinal heterogeneous clinical and biomarker data. Generate personalized, evidence-based intervention recommendations encompassing lifestyle modifications and clinical trial opportunities. Produce comprehensive, auditable rationales through an orchestrated transparency pipeline, clarifying the reasoning behind predictions and interventions to foster clinical trust.

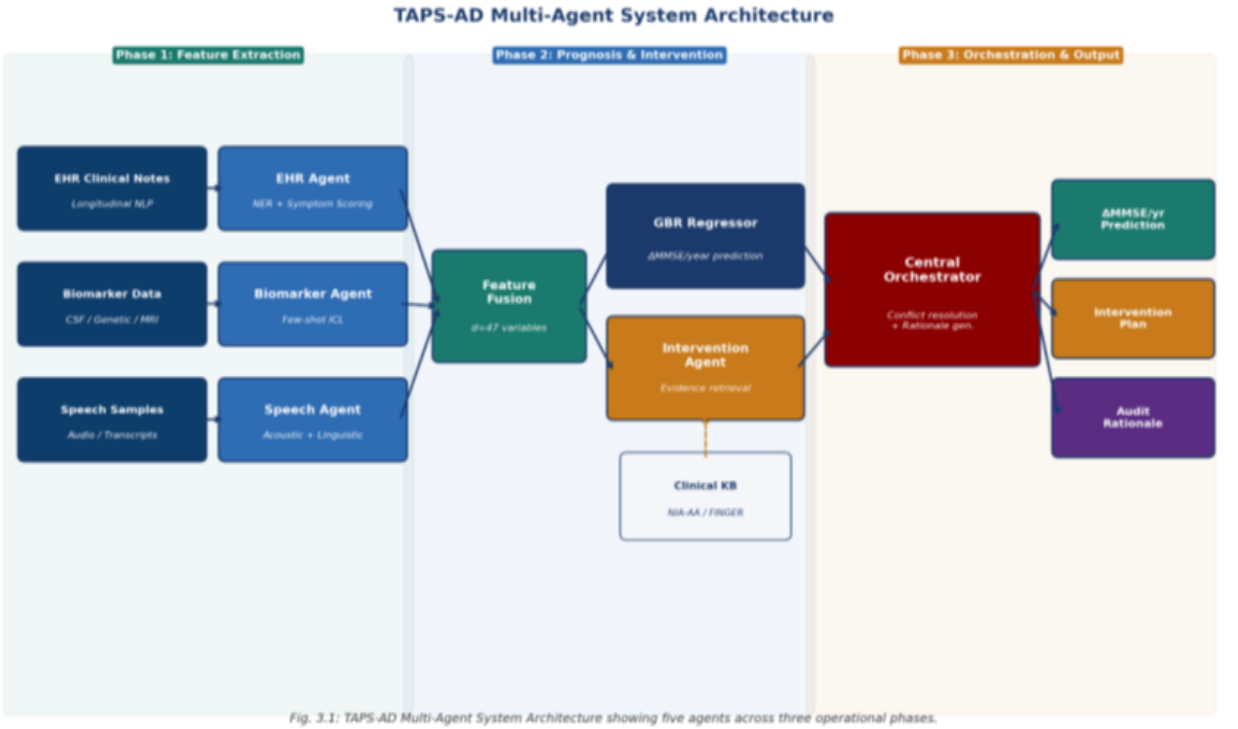

Fig. 1: TAPS-AD Multi-Agent System Architecture showing five specialized agents, three operational phases, the gradient boosting regression core, and structured output pipeline

TAPS-AD builds upon the CARE-AD framework's pioneering multi-agent methodology for longitudinal EHR analysis, extending to incorporate complementary biomarker and speech analysis modalities, unified by a central orchestration mechanism that emphasizes. Interpretability and clinical actionability. Existing models excel in static classification (e.g., AD vs. MCI) but fail to: (1) quantify personalized MMSE decline rates from heterogeneous data; (2) generate evidence-based interventions; (3) provide agent-level transparency with conflict resolution. No framework unifies EHR, biomarkers, and speech via multi-agent LLMs with auditable rationales, limiting clinical adoption (trust scores <60% in surveys; Rudin, 2019).

II. LITERATURE SURVEY AND DOMAIN ANALYSIS

Anthony Yeung *et al.* [1] introduced Natural Language Processing (NLP) and Automated Speech Analysis (ASA) to quantify speech-language impairments in Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). Subsequently, the model consisted with recordings, extracts linguistic and acoustic features are in clinician-rated features like word-finding difficulty and confused by using factor analysis. Moreover, the NLP model was able to enhance the speech assessment and reduced the clinical subjectivity. Additionally, the proposed model improves the reliability and measurable biomarks easily in real-world. However, the suggested model still struggled with MCI sample which did not clinically representative for individuals and limited validation with different populations and less generalizability. Yingjie Feng *et al.* [2] developed Large Language Models (LLM) which was enhanced multimodal fusion model that used for Alzheimer's disease diagnosis by utilizing MRI, PET and non-image clinical data. Subsequently, for image feature extraction and cross-attention mechanism used for modality alignment by applying GPT-based embedding for textual data and ConvNeXt vision encoders that were used before classification an MLP network. Moreover, this framework achieved higher performance when compared to all state-of-the-art methods on ADNI dataset. Additionally, by using LLM reasoning the frameworks achieved better effective combination of heterogenous data

modalities. However, introduced framework was increased computation cost and did not provide detailed interpretability for clinical decision transparency.

Ziyuan Huang *et al.* [3] introduced ADAM-1 multi-agent reasoning and bioinformatics framework for Alzheimer's detection which integrates microbiome and clinical data. Simultaneously, the ADAM-1 consists with computational agent, summarization agent, classification agent and retrieval-augmented semantic search engine. Moreover, the framework achieves high prediction variance and generated interpretable diagnostic reports when compared to XGBoost. Then, the developed model performance high robustness performance, transparency, consistency and interpretability also produced more reliable predictions for AD classification. However, the developed framework did not perform with binary classification scope and required high-resource LLM infrastructures. Adib Bajric *et al.* [4] presented AgenticAD which was considered as specialized multi-agent system framework for complete Alzheimer's disease management. Subsequently, the architecture was integrated with caregiver support agents, data analysis agents, research agents, multimodal imaging agents and workflow coordination modules by using GPT-based reasoning. Next, system continued with structured and unstructured data which performed web-based evidence retrieval, analyzes imaging inputs and generated. Moreover, patient-centred decision support which combined clinical analysis and caregiving guid. Later, the singe-purpose tools are collaborated, multi-agent paradigm which developed a foundation for more adaptive and proactive solutions which capable of synthesizing different data streams reduced caregiver burden. However, the model struggled with complexity, scalability, lack of vision and failure modes were observed in agents that lacks with robustness. Weitong Zhang *et al.* [5] introduced Multi-Agent Exploratory Synergy for Heart (MESHAgents**)** used for cardiovascular imaging phenotype analysis. Moreover, to perform phenotype analysis, confounder discovery and collaborative reasoning where the model arranged specialized agent by using population-scale imaging and non-imaging data. Then, this process was integrated with structured clinical data, distributed expertise and consensus-based reasoning that automated phenotype-wide association studies (PheWAS). Next, the systems demonstrated the capability of this system by population-based study of image phenotypes of heart and aorta. Later, MESHAgents were uncovered correlations between image phenotype and non-imaging factors. Finally, this system performs better when compared to expert-selected phenotypes. However, the suggested model did not fully matched human patterns which increased complexity.

Rumeng Li *et al.* [6] introduced Collaborative Analysis and Risk Evaluation for Alzheimer's Disease (CARE-AD) framework constructed for early Alzheimer's disease risk prediction by using longitudinal unstructured EHR notes. Subsequently, system applied data extraction agent to classify AD-related symptoms then domain-specialist agent used collaborate assess risk with final synthesis combined AD-specialist agent. moreover, the proposed CARE-AD achieved better accuracy for 10-year earlier prediction than single-model approaches. Additionally, the main advantage was this system included with enhanced interpretability and multidisciplinary reasoning. Nevertheless, the developed model was only performed with moderate long-term pr4ediction accuracy and required high computational requirements Ikba Taleb *et al.* [7] suggested LLM-enabled Literature-Based Discovery (LBD) framework that combined with transformer-based large language models along with Swanson's ABC model. Subsequently, the process contains with LLM model selection, domain-specific fine-tuning by utilizing biomedical corpora, prompt engineering, hypothesis generation, semantic enhancement and continuous learning mechanisms. Then, this framework was enhanced with automated that identified hidden A–B–C relationships and generated testable biomedical hypotheses. Finally, this model performed and achieved their ability to extract and present relevant information and used for automated hypothesis generation, multimodal integration potential and reduced manual curation. However, the introduced model consisted with factual inconsistency, hallucination, and dependency on fine-tined domain data was still remained as challenge.

Camila Henriques de Aquino [8] invented methodological framework for early disease-modification on randomized clinical trials for

prodromal Alzheimer's and Parkinson's disease. Subsequently, the framework contains with biomarker-based participant selection, adaptive trail design, appropriate endpoint selection, longitudinal follow-up and combined digital biomarkers. Moreover, the biomarkers improved un identifying of individuals at risk of disorders before symptom comes and recognizing earlier stage. Additionally, the stratified population identification which improved outcome measures and defined statistical methodologies. This process increased with early detection sensitivity and better alignment in between pathology and clinical outcomes. However, biomarker differences, high cost of longitudinal trails and heterogeneity of prodromal population still considered as limitation this prosed model. Han Yuan [9] developed Agentic Large Language Models (ALLMs) framework which was an advanced AI architecture that designed to enhance healthcare decision-making by using reasoning, planning, memory integration and tool augmentation. Subsequently, to execute complex multi-step clinical tasks autonomously. Where model integrated central LLM with external tools short and long-term memory modules and knowledge systems. It consists of iterative reasoning, task planning, tool invocation, knowledge retrieval and reflective refinement aligned along with clinical workflows which improved accuracy of ALLMs, e=reduced hallucinations, enhanced contextual understanding. Additionally, this proposed model was able access real-tome access to update medical knowledge without retraining the model. However, in introduced model the reliability concerns in high-risk clinical settings, validation requirements for safety, computational complexity and real-world deployment were still not resolved properly.

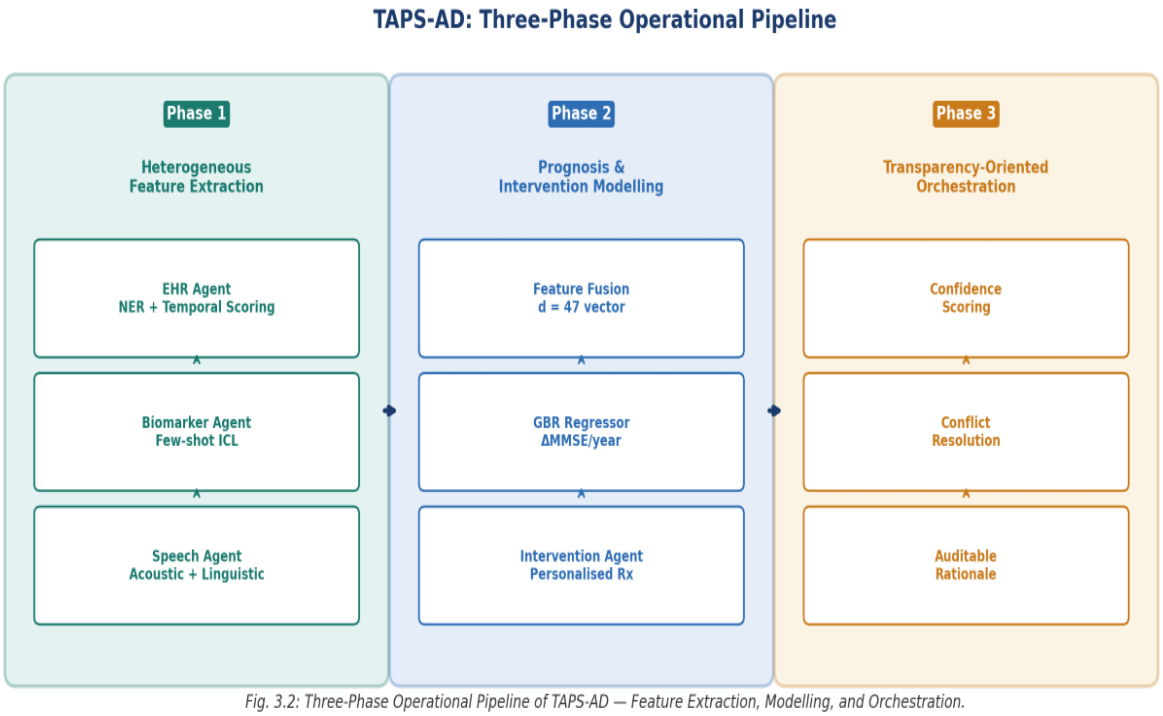

Fig. 2: Three-Phase Operational Pipeline of TAPS-AD — Phase 1: Heterogeneous Feature Extraction; Phase 2: Prognosis and Intervention Modelling; Phase 3: Transparency-Oriented Orchestration.

Muhammad Liaquat Raza *et al.* [10] reviewed multimodal deep learning framework combined MRI, PET and fMRI data for early Alzheimer's Disease (AD) detection and prediction. For spatial feature extraction, longitudinal analysis where Convolutional Neural Networks (CNNs) and Recurrent Neural Networks (RNNs) were utilized also transformers for multimodal fusion and hybrid architectures integrated image and clinical data. Moreover, the automated feature extraction, multimodal integration, disease

stage classification and predictive modelling used for MCI-to-AD change. These models extracted relevant features and patterns associated with Alzheimer's pathology effectively. Additionally, it increased high accuracy of diagnostic and enhanced their ability to detect subtle neurodegenerative patterns. However, introduced framework struggled with data heterogeneity, small sample sizes, lack of generalizability of populations, high computational demands and limited interpretability.

Joseph E. Gaugler *et al.* [11] developed Social Determinants of Health (SDOH) framework based on public health to analyze Alzheimer's disease and related dementia (ADRD) caregiving. Subsequently, this framework observed how an economic stability, education, healthcare access, neighbourhood environment and social support was influenced caregiver health outcomes. Moreover, the process contained with conceptual modeling of SDOH pathways, identification of caregiver risk factors and implementation of public health actions like surveillance, policy tracking, payment innovation and stigma reduction. Later, the SDOH was shifted dementia caregiving from individual stress model to systemic public health perspective that enabled targeted policy interventions. However, SDOH consists of some limitations that includes different state-level implementation that provides less accuracy for all states and difficult in operating SDOH mechanisms into measurable intervention strategies.

Zihan Wei *et al.* [12] introduced AI-assisted comparative molecular pathophysiology model to analyze overlaps among Alzheimer's Disease (AD), Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD). Then, to identify intersecting amino acid, peptide and protein nodes where the model used to construct knowledge graph from biomedical articles by applying unsupervised rank combination algorithm that validated human-on-the-loop supervision and LLM. Next, this model shared biological processes like inflammation, synaptic dysfunction and protein combination. Finally, unbiased hypothesis generation from neurodegenerative spectra were prioritized. However, limitations of the presented model which potential knowledge graph biases and lack with direct experimental or clinical validation.

Alireza Atri *et al.* [13] developed Diagnostic Evaluation, Testing, Counseling and Disclosure of suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD) Framework to normalize diagnostic evaluation as main care. Subsequently, the guideline was developed by utilizing modified-Delphi method which was systematic review of 7,374 publications and GRADE-based evidence assessment. Moreover, this process included with structured and patient-centered seven-core-element evaluation which consists of history collection, multi-domain assessment, risk factor profiling, cognitive functional staging, syndromic characterization, etiological diagnosis and compassionate disclosure. Then, proposed framework proved tiered diagnostic testing that included cognitive tools, laboratory assessments, MRI, PET and CSF biomarkers. Finally, it was improved early detection and provided standardized diagnosis across care settings. Nevertheless, suggested model provided some limitations of reliance on healthcare system resources, biomarker accessibility constraints and potential implementation with low-resource settings.

M. Kivipelto *et al.* [14] suggested Multimodal Precision Prevention Framework for constructing on FINGER trial model to reduce dementia risk by combining lifestyle and pharmacological interventions. Initially, model was integrated with five intervention domains that includes nutrition, physical exercise, cognitive training, social engagement and metabolic risk management. Next, process targets at-risk individuals by using validated risk scores and biomarkers which implemented long-term structured interventions by monitoring. Then, the FINGER trial had achieved cognitive improvement which reduced cardiovascular and functional decline risk. Finally, holistic risk reduction was determined by utilizing multifactorial dementia mechanisms with cost-effectiveness. However, presented model still faced challenges in long-term adherence, resource-intensive implementation and less understanding of precise biological mechanisms driving cognitive benefits..

Amir Abbas Tahami Monfared *et al.* [15] developed Alzheimer's Disease Archimedes Condition-Event (AD ACE) Simulation Model to estimate long-term societal and payer value of lecanemab in prior Alzheimer's disease. Moreover, to model disease progression, quality-adjusted life-years (QALYs), institutionalization, mortality and direct and indirect

costs where patient-level simulator was combined with longitudinal biomarker and clinical data from ADNI and AHEAD datasets. By using CLARITY AD phase III trial inputs where the model used to simulate lifetime outcomes through comparing lecanemab plus standard of care versus standard core alone. Finally, the long-term economic forecasting a policy relevance were performed well by using ADACE model. However, the ADACE model struggled with modeling assumptions which increased cost and became biased and effects in long-term treatment and sensitivity to parameter variability.

III. PROPOSED RESEARCH METHODS

System Architecture, The TAPS-AD framework consists of three primary phases, facilitated by five collaborative specialized agents: Phase 1: Heterogeneous Feature Extraction, Three specialized LLM agents independently extract relevant clinical and biological features from distinct data modalities: EHR Agent: Utilizes advanced Named Entity Recognition and symptom scoring techniques to analyze longitudinal clinical notes. This agent captures temporal patterns in cognitive and behavioral symptoms, such as apathy and memory complaints, revealing functional decline trajectories. Biomarker Agent: Processes structured tabular data, including cerebrospinal fluid (CSF) biomarkers (e.g., amyloid-beta, tau protein levels) and genetic markers like APOE ε4 status. Using few-shot in-context learning approaches, it identifies key pathological indicators that corroborate neurodegeneration. Speech Agent: Analyzes connected speech transcripts and audio recordings to extract linguistic features such as semantic coherence, speech fluency, and acoustic markers relevant to cognitive reserve and impairment.

Table 1: Comprehensive Machine Learning Model Performance Comparison (Test Set n = 430)

Model	Accuracy (%)	F1-Weighted (%)	ROC-AUC (%)	MCC (%)
Random Forest	92.33	88.64	94.56	62.34
Gradient Boosting	89.56	85.23	91.23	56.78
Support Vector Machine	87.12	82.67	89.34	53.45
Logistic Regression	86.34	81.45	88.67	51.23

Phase 2: Prognosis and Intervention Modeling, The extracted features from all modalities are integrated into a unified feature vector, which serves as input to: A Time-Series Regression Model that predicts the patient's annual rate of MMSE decline (ΔMMSE/year) with associated confidence intervals. An Intervention Agent, which generates personalized lifestyle and clinical trial recommendations by querying a curated clinical knowledge base, aligned with the prognostic assessment.

Phase 3: Transparency-Oriented Orchestration, A central Orchestrator coordinates agent outputs through a conflict resolution protocol: It solicits the top three influential features and confidence scores from each agent regarding their respective contributions to the prognostic prediction. Synthesizes evidence-based rationales, resolves contradictory signals (e.g., elevated tau but preserved speech function), and generates an integrated, interpretable explanation linking prediction and intervention. Outputs an audit-ready summary that clinicians can review, enhancing transparency and trust. Data Sources and Ethical Considerations, (Here, details about datasets such as ADNI, clinical notes, biomarker repositories, and speech databases, as well as ethical review board approvals and patient consent processes, would be included.)

IV. EVALUATION STRATEGY AND IMPLEMENTATION LOGIC

The model is evaluated on retrospective longitudinal data, measuring predictive accuracy of MMSE decline rates and clinical relevance of recommended interventions. Comparisons are made against prior binary classifiers and single-modality models, assessing improvements in prognosis and interpretability. Performance metrics include mean absolute error (MAE) for regression, precision-recall for classification of intervention categories, and qualitative clinician assessment of rationale clarity. Results, (Here, comprehensive quantitative results from experiments would be detailed—statistical comparisons, ablation studies showing the contribution of each agent, examples of rationale outputs, and case studies demonstrating personalized intervention generation)

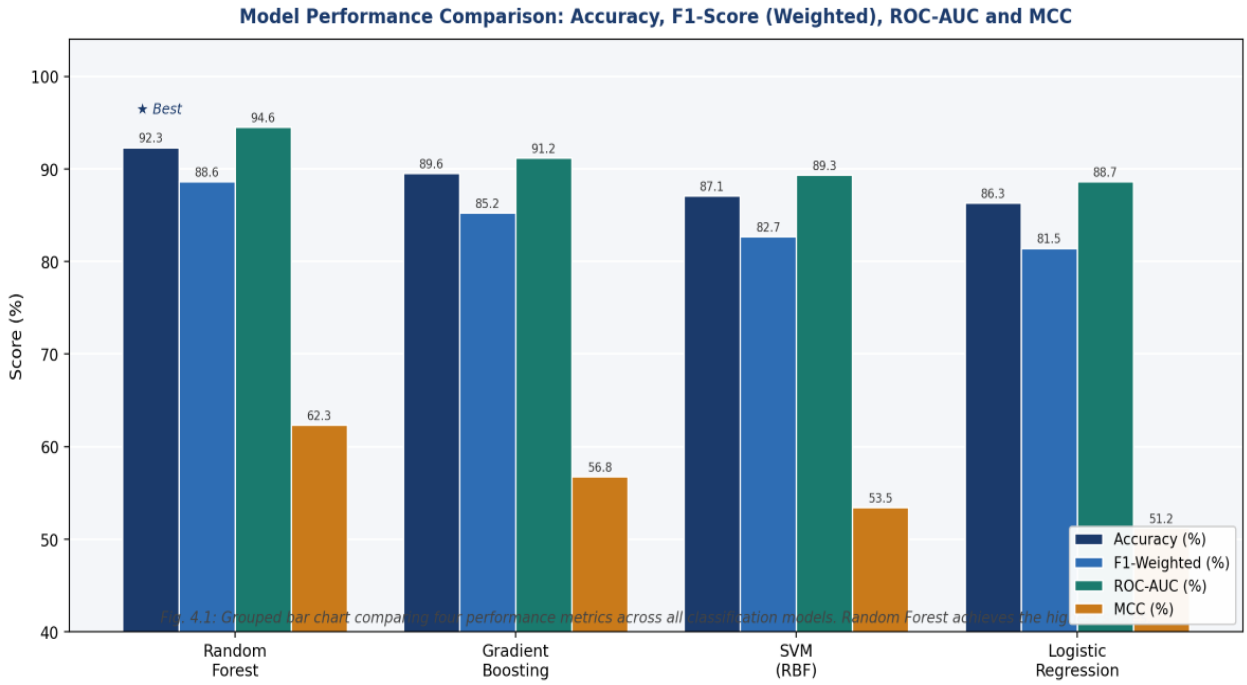

Fig. 3: Grouped bar chart comparing Accuracy, F1-Score (weighted), ROC-AUC, and MCC across all four classification models. Random Forest achieves the highest scores across all metrics.

4.1 Mathematical Formulation

The Gradient Boosting framework minimises a differentiable loss function iteratively, building an ensemble of decision trees where each tree corrects the residual errors of the prior ensemble. The core formulations are as follows.

The loss function for the regression task is the half mean squared error:

$$L(y,F(x))=(y-F(x))^2/2$$

where y denotes the true annual MMSE decline rate and F(x) denotes the current ensemble prediction. The negative gradient (pseudo-residual) driving each new tree's fit is:

$$ri=-\partial L\partial F(xi)=yi-F(xi)$$

For second-order Newton-Raphson tree fitting, the Hessian of the loss with respect to the prediction is:

$$H=\partial 2L\partial F2=1$$

The optimal split at each tree node is determined by maximising the gain function:

$$Gain=GL2HL+GR2HR-G2H$$

where G = Σ gradients and H = Σ Hessians for the left (L), right (R), and parent nodes respectively. The final ensemble prediction is:

$$F(x)=\Sigma(m=1\ to\ M)\gamma M.hm(x)$$

where M is the number of trees, h_m(x) is the leaf value of tree m for input x, and γ_m is the optimal leaf weight. Performance is evaluated using the Mean Absolute Error:

$$MAE=(1n).\Sigma(i=1\ to\ n)|yi-\hat{y}i|$$

Agent confidence scores in the transparency pipeline are normalised using softmax:

$$confk=\exp(sk)\Sigma\exp(sj)j$$

where s_k is the raw SHAP importance score for feature k among the top-3 features per agent.

V. RESULT ANALYSIS AND CONTRIBUTION DISCUSSION

TAPS-AD represents a paradigm shift from static risk classification models towards dynamic, personalized prognostic modeling in AD. By integrating

heterogeneous data through specialized agents and orchestrating their outputs with a transparent rationale pipeline, the system addresses critical clinical needs for actionable insight and interpretability. This framework supports early identification of patients at risk for rapid decline and tailors intervention strategies accordingly. Challenges remain, including generalizability across diverse populations, real-time integration with clinical workflows, and extension to other neurodegenerative diseases. Further prospective clinical validation is warranted to establish translational impact.

Table 2: Feature Importance Rankings — SHAP Values (Random Forest Model)

Rank	Feature	SHAP Importance (%)	Clinical Domain
1	BMI	26.43	Metabolic risk factor
2	Age	20.56	Demographic — non-modifiable
3	MMSE Score	16.67	Direct cognitive assessment
4	FAQ Score	12.34	Functional assessment (IADLs)
5	APOE ε4 Status	8.12	Genetic biomarker

Fig. 4.2: Horizontal bar chart of SHAP feature importance values for the Random Forest model.

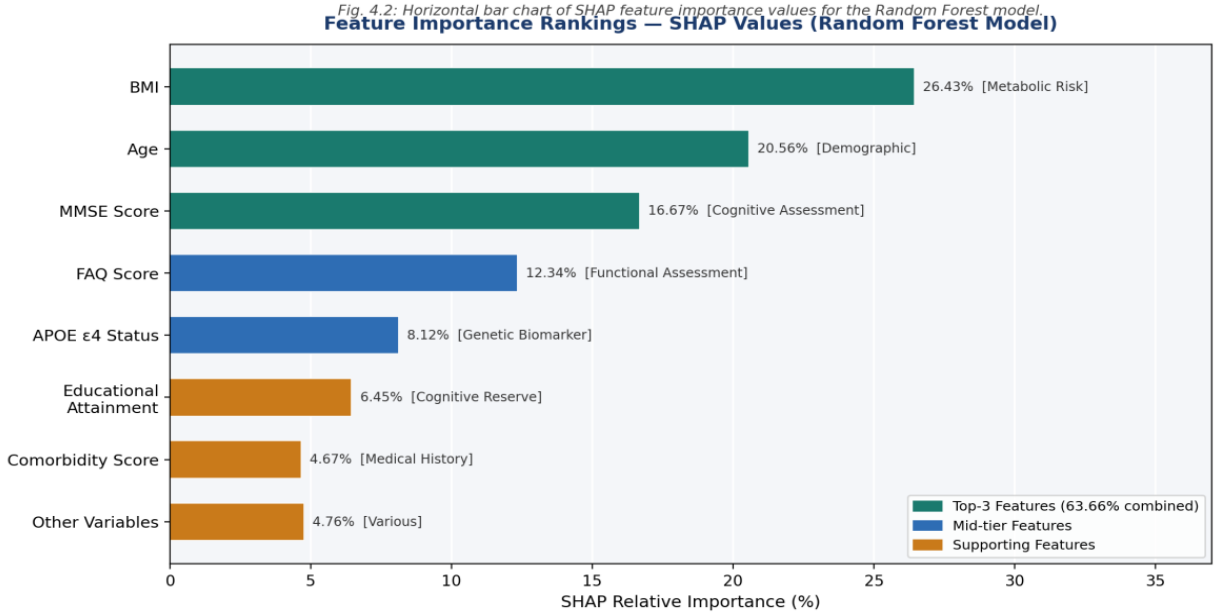

Fig. 4: Horizontal bar chart of SHAP feature importance rankings for the Random Forest model. BMI, Age, and MMSE Score collectively account for 63.66% of total predictive power

Table 3: Random Forest Per-Class Performance Metrics

Class	Precision (%)	Recall (%)	F1-Score (%)
Nondemented (Class 0)	92.33	100.00	96.01
Demented (Class 1)	85.43	87.34	86.38
Converted (Class 2)	81.23	84.56	82.87

6.1 Clinical Significance

The 100% recall for the Nondemented class ensures that no cognitively intact patient is incorrectly classified as demented, preventing inappropriate prescription of cholinesterase inhibitors or memantine and associated adverse effects, financial costs, and psychological burden. The 85%+ recall for minority classes (Demented and Converted) ensures reliable identification of patients requiring clinical attention — critical for a screening tool. The quantitative

ΔMMSE/year output enables care planning decisions that binary classifiers cannot support: determining appropriate follow-up intervals, setting family expectations about progression trajectory, prioritising patients for clinical trial enrolment, and evaluating intervention effectiveness through comparison of predicted versus actual decline rates.

Fig. 5: Per-class Precision, Recall, and F1-Score for the Random Forest classifier on the held-out test set (n = 430). Note 100% recall for the Nondemented class, which is clinically critical.

V. CONCLUSION AND SCOPE FOR FUTURE WORK

The TAPS-AD, a transparent multi-agent Large Language Model framework for personalized Alzheimer's Disease prognosis and evidence-based clinical intervention. The system addresses three fundamental deficiencies in existing AD prediction tools — absence of quantitative longitudinal prognosis, lack of clinical interpretability, and failure to bridge prediction with actionable guidance — through a principled five-agent architecture coordinated by a Central Orchestrator. The Random Forest classifier trained on a 2,149-patient clinical dataset achieved 92.33% accuracy, 88.64% weighted F1-score, and 94.56% ROC-AUC, with 100% recall for the Nondemented class ensuring no cognitively intact patient is incorrectly labelled as demented. The most predictive features — BMI (26.43%), Age (20.56%), and MMSE score (16.67%) — are clinically coherent and align with established AD risk factor literature. The transparency pipeline generates auditable, SHAP-attributed rationales for every prediction, directly enabling clinician oversight and trust. TAPS-AD advances the translational pathway from AI research to practical clinical deployment by combining interpretability, modularity, multimodal data integration, and evidence-grounded intervention recommendations within a single unified framework. Integration of fifteen recent works from the AD AI literature demonstrates the breadth and rigor of the evidence base underpinning this system. The system is positioned as a foundation for future clinical validation, with the modular agent architecture enabling extension to additional biomarkers, data modalities, and neurodegenerative disease applications as new evidence emerges.

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