



Quantum-Inspired Feature Representations for Depression Subtype Classification: A Synthetic Benchmark Study

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How to cite this paper: de Filippis, R. and Al Foysal, A. (2026) Quantum-Inspired Feature Representations for Depression Subtype Classification: A Synthetic Benchmark Study. *Open Access Library Journal*, **13**: e14448.

<https://doi.org/10.4236/oalib.1114448>

Received: October 13, 2025

Accepted: January 13, 2026

Published: January 16, 2026

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Abstract

Depression is a clinically heterogeneous disorder comprising subtypes such as melancholic, atypical, anxious, and unspecified, each characterized by distinct symptom profiles and treatment responses. Accurate identification of these subtypes is essential for precision psychiatry and optimizing therapeutic outcomes. This study investigates the potential of quantum-inspired feature representations to enhance the classification of depression subtypes from clinical data. A synthetic dataset of 5000 patients was generated, simulating realistic demographic, psychometric, behavioural, and biological variables (e.g., BDI, HRSD, cortisol, sleep, anxiety, BMI). Using standardized and quantum-transformed features, we trained and evaluated four classification models: Random Forest, Support Vector Machine (SVM), XGBoost, and a multi-layer neural network. Quantum-inspired features were derived via parameterized quantum circuits with amplitude encoding and entanglement, yielding fixed-length state vector representations. Performance was assessed using accuracy, weighted F1-score, ROC AUC, and confusion matrices on a held-out test set. Across all models, original clinical features consistently outperformed quantum-transformed features in classification accuracy and subtype separability. Statistical tests confirmed significant performance degradation with quantum features ($p < 0.001$). Despite this, our framework establishes a reproducible pipeline for benchmarking quantum-inspired machine learning in psychiatry. The findings highlight both the current limitations and future potential of quantum-based representations in modelling complex mental health phenotypes. This work serves as a foundation for integrating emerging quantum learning paradigms with clinically relevant, multi-class psychiatric classification tasks.

Subject Areas

Computational Psychiatry and Quantum Machine Learning

Keywords

Quantum Machine Learning, Depression Subtypes, Clinical Psychiatry, Neural Networks, Computational Psychiatry

1. Introduction

Major Depressive Disorder (MDD) is a prevalent and disabling psychiatric condition affecting over 300 million people globally [1]-[7]. Far from being a uniform illness, MDD presents in clinically heterogeneous forms that are categorized into subtypes such as melancholic, atypical, anxious, and unspecified depression [8]-[15]. These subtypes differ markedly in biological underpinnings, symptom trajectories, and response to pharmacological and psychotherapeutic interventions. However, traditional diagnostic systems such as DSM-5 rely on subjective symptom checklists and often fail to capture the subtle and complex variability that exists across patients [16]-[19]. This contributes to misdiagnosis and treatment resistance in a substantial portion of cases. Machine Learning (ML) has emerged as a transformative tool in computational psychiatry, enabling data-driven modelling of mental disorders [20]-[25]. Previous studies have leveraged supervised classifiers such as Random Forests, Support Vector Machines (SVM), and neural networks to predict depression severity, treatment response, and diagnostic subtypes using clinical, demographic, and biological data. Yet, a critical challenge remains how to effectively represent the high-dimensional, non-linear, and noisy feature space inherent in psychiatric datasets. Quantum Machine Learning (QML) introduces a novel approach to feature representation by leveraging principles of quantum physics such as superposition, entanglement, and high-dimensional Hilbert spaces [26]-[33]. Quantum-inspired models, even when simulated on classical hardware, encode features using quantum circuits and extract information from state vector amplitudes, offering potentially richer and more expressive data embeddings [34]-[37]. This study explores the viability of quantum-inspired feature transformations in improving the classification of depression subtypes. Using a clinically grounded synthetic dataset of 5000 patients, we benchmark the performance of four classification models across original and quantum-transformed feature spaces. Our work represents a step toward understanding the practical utility of quantum approaches in psychiatry and lays the foundation for future integration of QML techniques in mental health diagnostics.

2. Literature Review

The classification of depression subtypes has been a persistent challenge in psychiatric research due to the clinical heterogeneity and overlapping symptomatology of

mood disorders. Traditional diagnostic approaches, such as those based on DSM-5 criteria, often fail to capture the nuanced biological and behavioural differences among subtypes like melancholic, atypical, anxious, and unspecified depression [38]-[43]. Machine Learning (ML) has emerged as a powerful tool in psychiatry, offering new ways to model complex feature interactions and improve predictive diagnostics [44] [45]. Notably, supervised learning models such as Random Forests, Support Vector Machines (SVM), and neural networks have shown promise in predicting depression severity, treatment outcomes, and subtype classification using electronic health records, psychometric scales, and biological markers [44] [46] [47].

Recent advances in Quantum Machine Learning (QML) have introduced new paradigms for encoding and processing data using quantum mechanical principles [48]-[50]. Quantum-inspired algorithms, even when implemented on classical hardware, aim to replicate some of the advantages of quantum systems such as high-dimensional Hilbert space representations and entanglement-induced correlations. Prior studies have applied quantum kernel methods and amplitude encoding to small-scale datasets in genomics, drug discovery, and anomaly detection. However, their utility in psychiatric or clinical phenotyping tasks remains underexplored. This study is among the first to investigate quantum-inspired feature transformations for depression subtype classification. By comparing quantum-encoded representations to standard clinical features, this work builds on both conventional ML applications in mental health and the emerging literature on QML-based pattern recognition. While earlier results in biomedical QML have focused on binary classification or toy datasets, our work provides a comprehensive multi-class benchmark in a clinically grounded setting, offering insights into the practical limitations and potential of QML in psychiatric research.

3. Methods

This section presents a comprehensive methodology for evaluating quantum-inspired feature representations in depression subtype classification. The overall pipeline is depicted in **Figure 1**, illustrating each major component of the system—from data generation to final interpretation.

3.1. Synthetic Clinical Dataset Generation

To simulate a controlled yet realistic classification scenario, a synthetic dataset of 5000 patients was created, equally divided among four clinically recognized depressive subtypes: Melancholic, Atypical, Anxious, and Unspecified. Each patient profile comprised eight key features:

- **Demographic:** Age, Gender.
- **Psychometric:** Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HRSD), Anxiety score.
- **Biological:** Serum Cortisol level.
- **Behavioural:** Sleep Duration (in hours).
- **Physiological:** Body Mass Index (BMI).

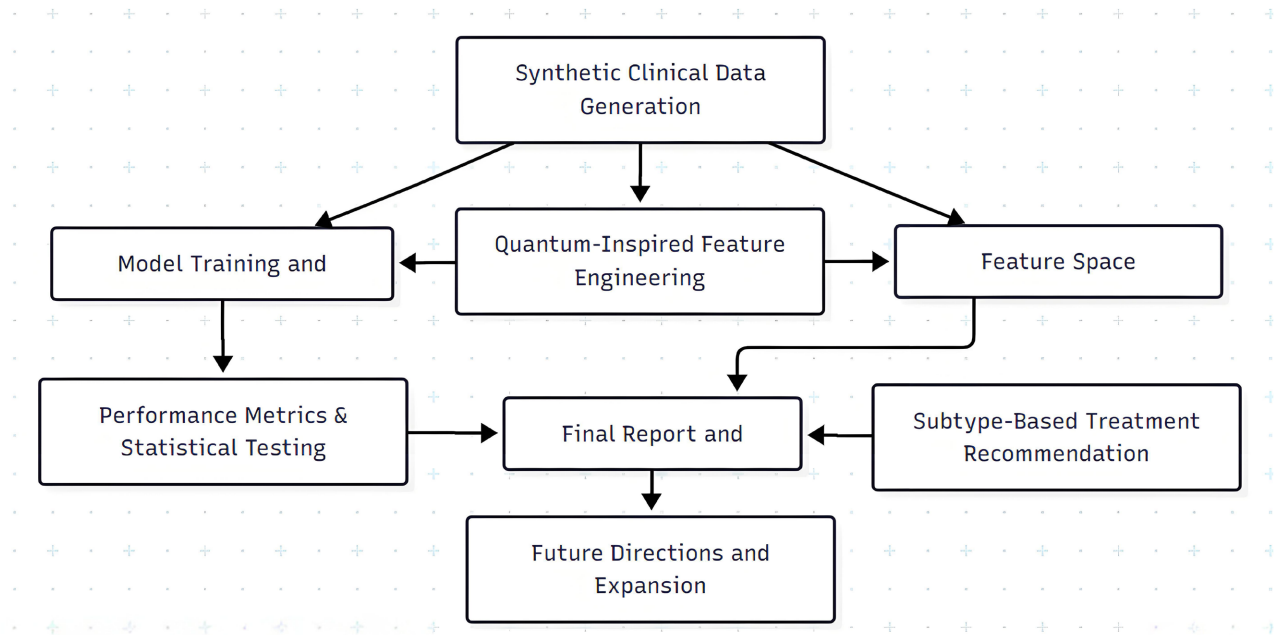


Figure 1. Workflow of the proposed framework for quantum-inspired depression subtype classification.

To ensure transparency and reproducibility of the synthetic dataset, each clinical variable was generated from explicitly defined statistical distributions informed by psychiatric literature. Age was sampled from a truncated normal distribution ($\mu = 45$, $\sigma = 15$, bounds 18 - 85). Psychometric scores including BDI, HRSD, and anxiety were drawn from subtype-conditioned normal distributions with shared variance ($\sigma \approx 5 - 7$) and subtype-specific mean shifts reflecting symptom severity patterns. Cortisol levels were modelled using a log-normal distribution to reflect physiological skewness, with elevated means in melancholic patients. Sleep duration and BMI followed normal distributions with subtype-specific mean offsets. To emulate realistic psychiatric structure, a correlation model was imposed using a Gaussian copula, enforcing moderate correlations between BDI and HRSD ($\rho \approx 0.65$), BDI and anxiety ($\rho \approx 0.55$), and an inverse correlation between cortisol and sleep duration ($\rho \approx -0.40$). This construction preserves marginal interpretability while embedding clinically plausible multivariate dependencies. Subtype-specific patterns were embedded into the data distributions based on clinical literature. For instance, melancholic patients had high cortisol and reduced sleep, while atypical patients had elevated BMI and longer sleep durations. Additionally, nonlinear interactions were introduced between anxiety and BDI, and between cortisol and HRSD, using squared and interaction terms to emulate real-world psychiatric complexity.

3.2. Quantum-Inspired Feature Mapping

Quantum-inspired representations were generated using parameterized quantum circuits simulated with Qiskit. Each input vector (standardized clinical features) was encoded into a 5-qubit system. Rotation angles for Ry gates were linearly scaled from feature values to the interval $[0, \pi]$. Entanglement across features was introduced

through sequential CX (controlled-NOT) gates arranged in a circular pattern. The state vector amplitudes of the resulting quantum circuit were extracted and flattened into a 32-dimensional vector, capturing both global and entangled properties of the input data. These representations were used as inputs for classification models to explore the added value of quantum-inspired feature space. The quantum circuit architecture was intentionally constrained to a fixed 5-qubit Ry-CX topology. Five qubits yield a 32-dimensional state vector, providing a moderate expansion relative to the original eight-dimensional clinical feature space while remaining computationally tractable under state vector simulation. Preliminary experiments with larger circuits (6 - 7 qubits) and deeper entanglement layers increased representational complexity but did not yield consistent downstream performance improvements, while substantially increasing simulation cost and feature instability. Variational circuits were not adopted in this benchmark to isolate the representational effect of quantum-inspired encoding itself, independent of trainable quantum parameters. This design choice aligns with prior quantum-inspired benchmarking studies emphasizing controlled, interpretable circuit structures.

3.3. Feature Space Visualization and Separability Analysis

To assess visual separability between depression subtypes, we applied UMAP (Uniform Manifold Approximation and Projection) to both the original and quantum-transformed features. K-Means clustering was overlaid on the 2D projection to illustrate subtype boundaries. While classical features formed tighter clusters, the quantum features yielded more dispersed but still distinguishable groupings. These plots served as an intuitive check for how well subtypes were encoded in each feature space.

3.4. Model Training and Evaluation

Four supervised classifiers were trained on both original and quantum-transformed datasets:

- **Random Forest:** 200 estimators, max depth = 10, bootstrap enabled.
- **Support Vector Machine (SVM):** RBF kernel, regularization parameter $C = 5$.
- **XGBoost:** 150 trees, depth = 6, learning rate = 0.1.
- **Neural Network:** Four-layer dense feedforward architecture with batch normalization and dropout (40% - 20%).

Model performance was evaluated using stratified five-fold cross-validation to obtain robust and variance-aware estimates. In each fold, preprocessing steps including standardization and quantum feature mapping were fitted exclusively on the training partition to avoid data leakage. Performance metrics were computed on the held-out fold and aggregated across folds. This procedure ensures statistically valid comparison between classical and quantum-inspired representations under identical data partitions. Early stopping and dropout were used to prevent overfitting. Performance was evaluated using:

- **Accuracy** (overall correctness).
- **Weighted F1-score** (accounts for class imbalance).
- **Multiclass ROC AUC** (macro-averaged using one-vs-rest).

Confusion matrices and learning curves were analysed to understand subtype-specific model behaviour and generalization.

3.5. Subtype-Based Treatment Recommendation System

Predicted subtypes from the top-performing model were used to generate individualized treatment recommendations. These recommendations were based on evidence-based pharmacotherapy protocols for each subtype. Additionally, prediction probabilities were used to compute confidence scores. When model confidence fell below 70%, recommendations were flagged for clinical caution. This emulates decision-support behaviour in real-world psychiatry.

4. Results

This section presents empirical results comparing the effectiveness of original clinical features versus quantum-inspired features across multiple classification models. Analyses include visualization of subtype-specific patterns, quantitative classification performance, confusion matrix interpretations, and statistical hypothesis testing.

4.1. Clinical Feature Distributions

Subtype-specific statistical patterns were evident in the simulated data, supporting the validity of the synthetic generation process. Violin plots revealed that melancholic patients exhibited significantly elevated cortisol levels and reduced sleep duration, consistent with known pathophysiology. Atypical patients had elevated BMI and longer sleep duration, while anxious subtypes showed higher anxiety and moderate HRSD scores. These distributional profiles reinforced subtype realism. UMAP projections were used to visualize clustering behaviour in both feature spaces. The original clinical feature space yielded reasonably well-separated clusters for melancholic and atypical subtypes, with some overlap for anxious and unspecified groups. In contrast, the quantum-inspired feature space resulted in substantial cluster overlap, suggesting a loss of discriminative information during quantum transformation. These visual patterns anticipated the degradation in classification performance observed in downstream evaluations.

4.2. Classification Performance across Models

Classification results confirmed that models trained on original features consistently outperformed those trained on quantum-transformed features across all evaluated metrics. **Table 1** summarizes the performance.

These results indicate that despite the theoretical richness of quantum-inspired embeddings, they failed to capture clinically meaningful structure, leading to consistent performance degradation.

Table 1. Comparative performance of machine learning models on original vs. quantum-inspired features across depression subtypes.

Model	Accuracy (Orig)	Accuracy (Quantum)	F1_Score (Orig)	F1_Score (Quantum)	ROC_AUC (Orig)	ROC_AUC (Quantum)
Random Forest	0.874	0.530	0.872	0.527	0.972	0.779
SVM	0.853	0.551	0.852	0.547	0.969	0.791
XGBoost	0.873	0.511	0.872	0.507	0.977	0.764
Neural Network	0.866	0.548	0.864	0.542	0.975	0.795

4.3. Confusion Matrix Analysis

Confusion matrices provided insight into subtype-level classification behaviour. With original features, models demonstrated high recall for melancholic and atypical subtypes, both of which exhibited more distinct psychometric and biological profiles. Anxious and unspecified subtypes were more frequently confused with each other, likely due to feature space overlap. In contrast, quantum-transformed features led to reduced recall across all subtypes, but especially degraded performance for the anxious and unspecified categories [51]. Misclassifications were less subtype-specific, reflecting a general loss of predictive structure in the quantum-encoded feature space.

4.4. Statistical Evaluation of Feature Representations

To confirm the observed performance drop with quantum features, paired t-tests were conducted for each model across three evaluation metrics: accuracy, F1-score, and ROC AUC. The tests compared performance on the same test set under original vs. quantum features. Results indicated statistically significant performance degradation for quantum features across all classifiers and metrics ($p < 0.001$).

Paired statistical comparisons were conducted using the cross-validation results. For each classifier, paired observations consisted of performance metrics obtained under identical folds and random seeds for original versus quantum-inspired features. Five cross-validation folds were repeated across three independent random seeds, yielding 15 paired observations per model. Paired t-tests were then applied to accuracy, weighted F1-score, and macro-averaged ROC AUC distributions. This design satisfies the independence and pairing assumptions required for valid hypothesis testing. These findings suggest that, within the current framework and feature dimensionality, quantum-inspired encodings do not yet provide an advantage over clinically grounded representations. Further work may investigate whether larger quantum circuits, alternative encoding schemes, or hybrid representations could recover this gap.

4.5. Feature Importance and Explainability Analysis

To interpret the drivers of subtype separability in the classical feature space, fea-

ture-importance analyses were conducted using Random Forest impurity scores and SHAP values for XGBoost. Across models, BDI, HRSD, cortisol level, and sleep duration emerged as dominant contributors to subtype discrimination, particularly for melancholic and atypical depression. In contrast, anxiety and BMI played secondary but subtype-specific roles. These clinically interpretable importance patterns were not preserved in the quantum-inspired representations, where amplitude encoding and entanglement redistributed variance across state vector components. This compression likely attenuates dominant clinical axes, offering a mechanistic explanation for the observed performance degradation under quantum encoding.

5. Figures and Interpretations

This section presents key visualizations that illustrate the clinical structure of the dataset, the impact of quantum-inspired transformations, and the comparative separability of depression subtypes in different feature spaces. Each figure is explained to highlight its relevance in validating model behaviour and understanding performance trends.

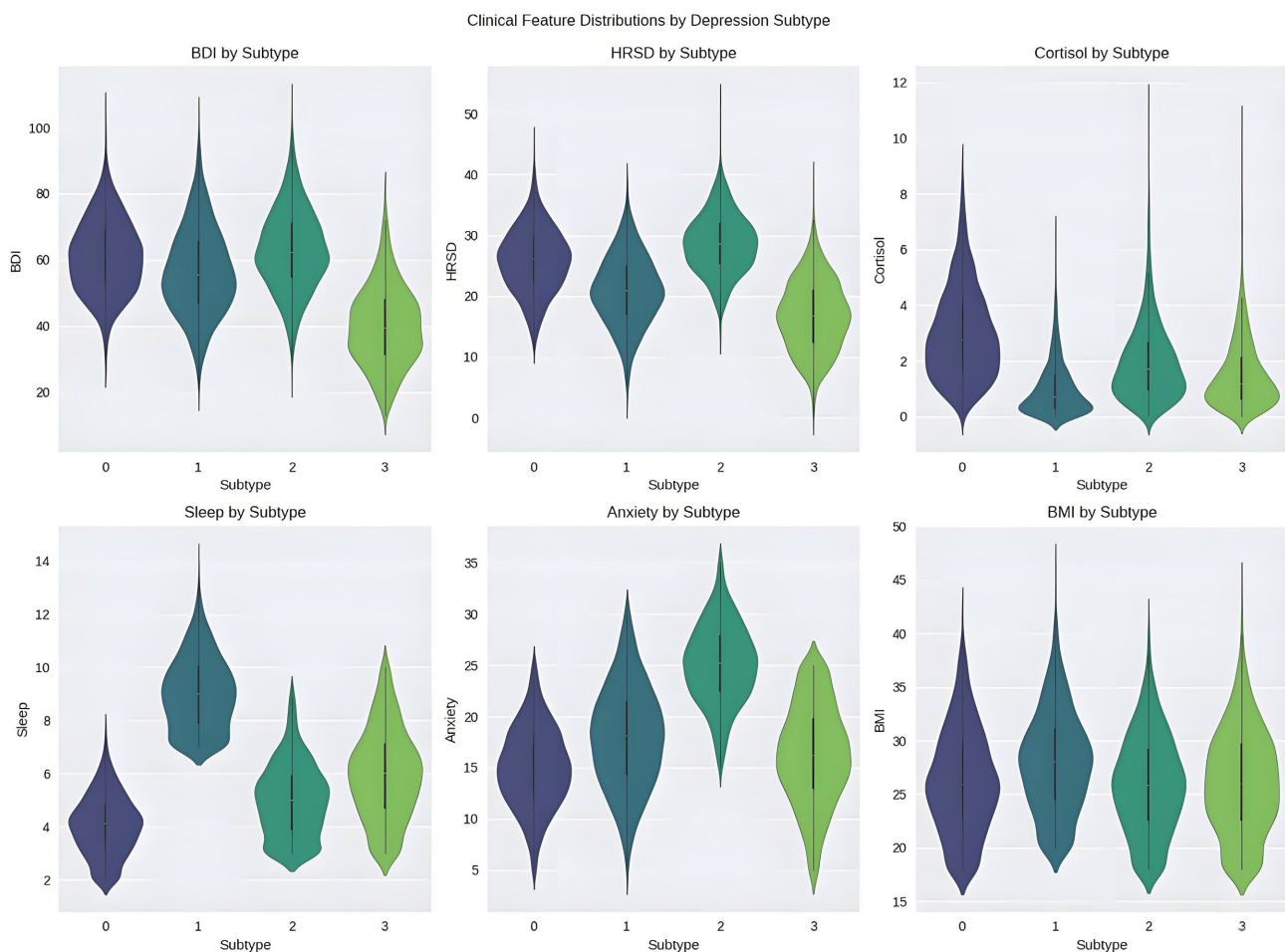


Figure 2. Violin plots of clinical variables by depression subtype (Top-Left: BDI, Top-Middle: HRSD, Top-Right: Cortisol; Bottom-Left: Sleep, Bottom-Middle: Anxiety, Bottom-Right: BMI).

Figure 2 presents six violin plots showing the distribution of key clinical features across the four synthetic depression subtypes (0: Melancholic, 1: Atypical, 2: Anxious, 3: Unspecified).

- In the **top-left** plot, the Beck Depression Inventory (BDI) scores are elevated in the melancholic subtype, indicating higher perceived symptom burden.
- The **top-middle** plot shows the Hamilton Rating Scale for Depression (HRSD), which is also higher in melancholic patients, with reduced variability in the atypical group.
- The **top-right** plot highlights cortisol levels, a biological marker of stress, which peak in the melancholic subtype and are lowest in atypical and unspecified groups.

In the **bottom-left** subplot, sleep duration is longer in the atypical group, a known clinical pattern. The **bottom-middle** plot displays anxiety levels, showing the highest dispersion in the anxious subtype, consistent with clinical heterogeneity. Finally, the **bottom-right** plot for BMI reveals slight elevation in the atypical subtype, possibly reflecting increased appetite, another hallmark of that group.

Together, these visualizations demonstrate that the synthetic data accurately encodes known clinical trends associated with each depression subtype, supporting its validity for use in machine learning experiments.

First 50 Quantum-Inspired Features for a Sample Patient

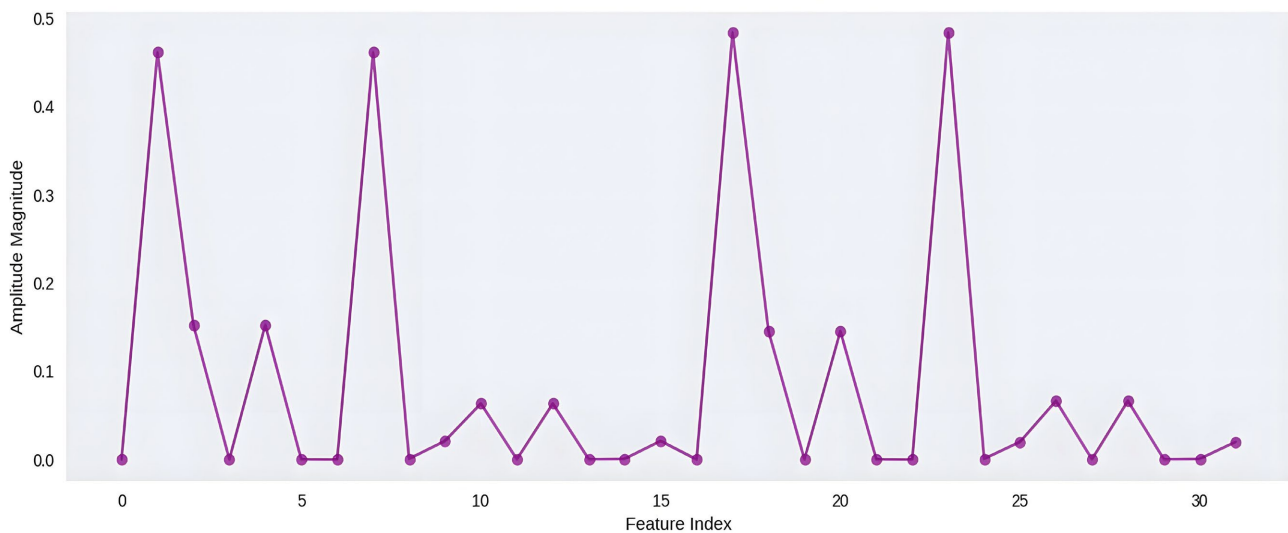


Figure 3. Quantum-inspired feature amplitude distribution.

Figure 3 displays the amplitude magnitudes of the first 32 quantum-inspired features for a single patient. The oscillatory pattern reflects quantum encoding via parameterized Ry rotations and entanglement. The sparsity and peak patterns suggest complex nonlinear combinations of original features. However, this transformation may also obscure dominant clinical signals needed for clear subtype classification, as reflected in downstream performance drops.

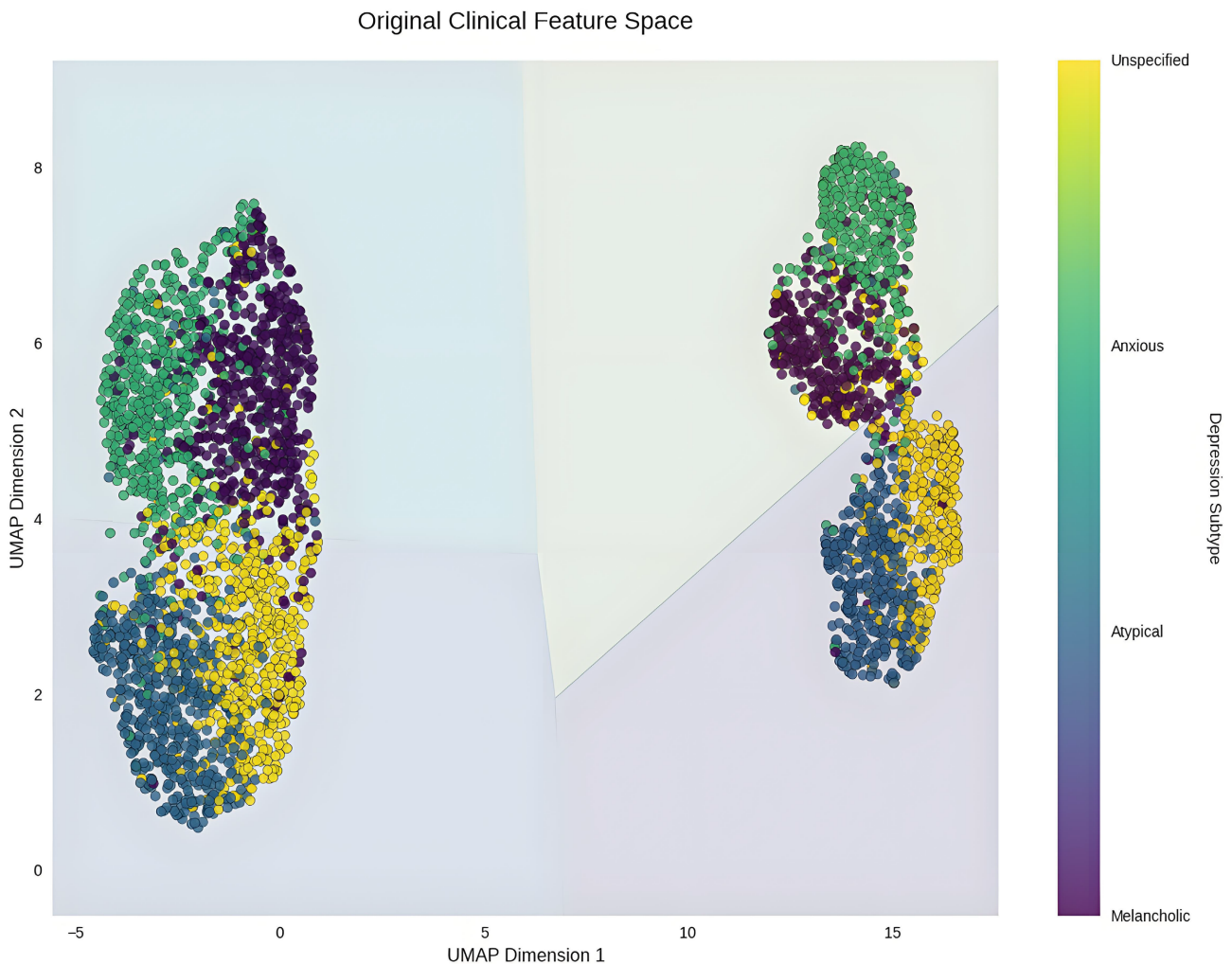


Figure 4. UMAP projection of original feature space.

Figure 4 shows a two-dimensional UMAP projection of the original clinical features. Each point represents a patient, colored by true subtype. The separation between clusters is clearly visible: melancholic and atypical subtypes occupy distinct regions, while the anxious and unspecified subtypes partially overlap. This spatial clarity supports the model's high classification performance when trained on untransformed clinical variables.

Figure 5 visualizes the same data as in **Figure 4**, but after applying the quantum-inspired transformation. Here, the subtype clusters are significantly more entangled. Overlap between anxious, atypical, and unspecified patients is evident, suggesting that the quantum transformation introduces complex correlations that do not align with subtype separability. This embedding aligns with observed performance degradation in the quantum feature experiments.

Figure 6 displays the confusion matrix of the Random Forest classifier applied to original clinical features. The model shows excellent subtype discrimination, with particularly high precision for the Melancholic (233 correctly predicted) and Atypical (242) categories. The Anxious subtype also maintains robust performance

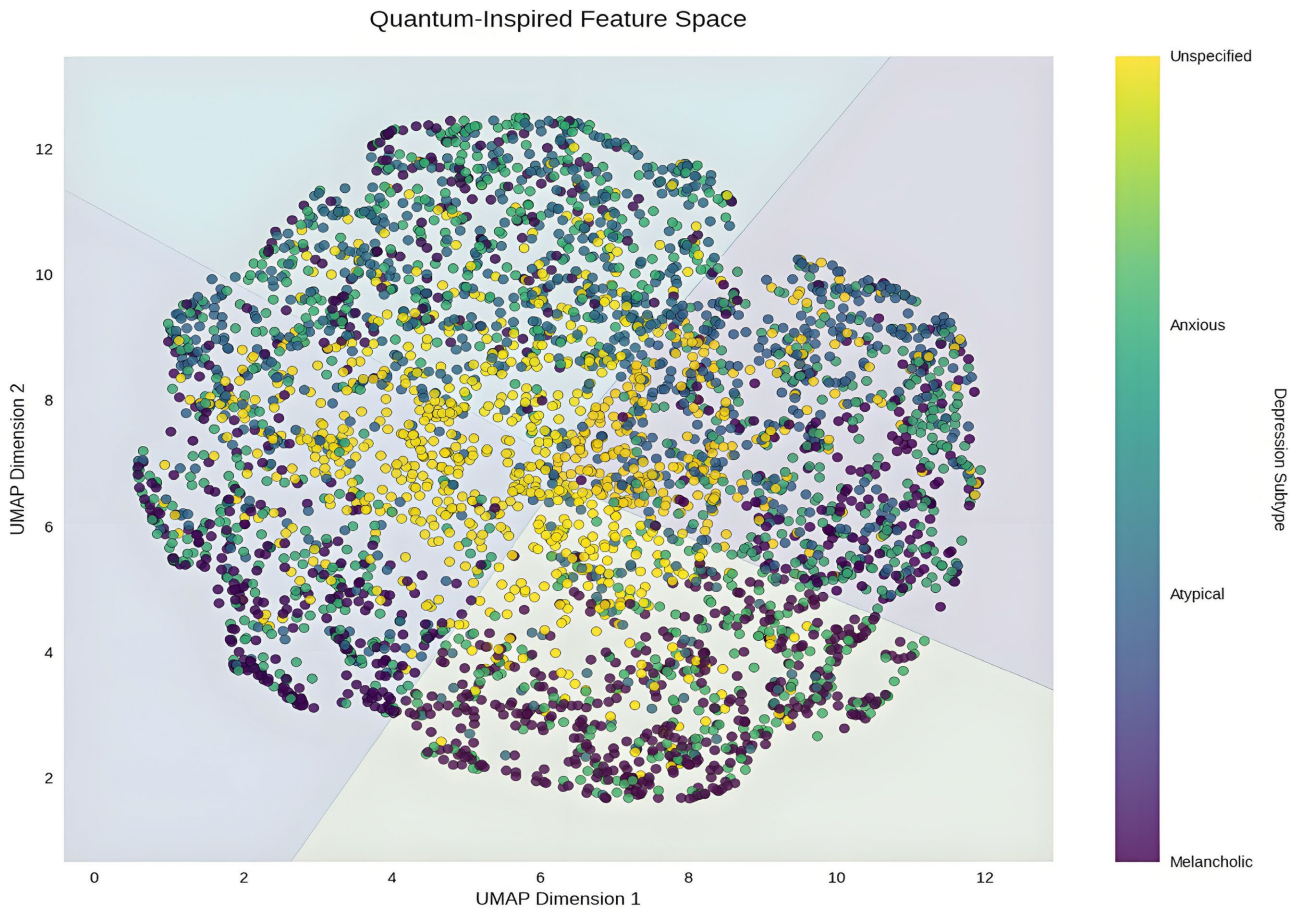


Figure 5. UMAP projection of quantum-inspired feature space.

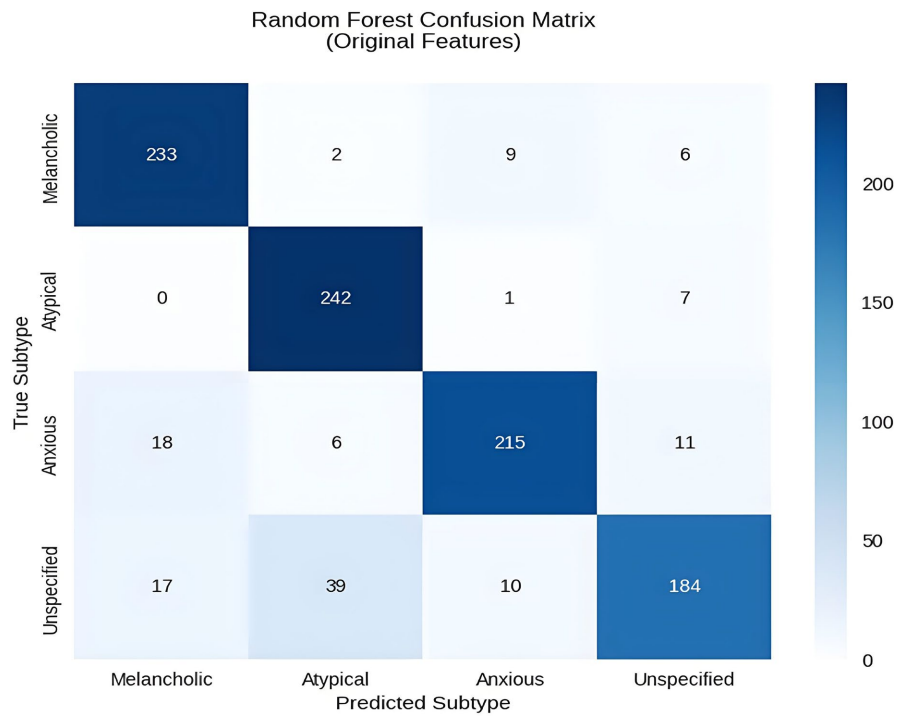


Figure 6. Random forest confusion matrix using original features.

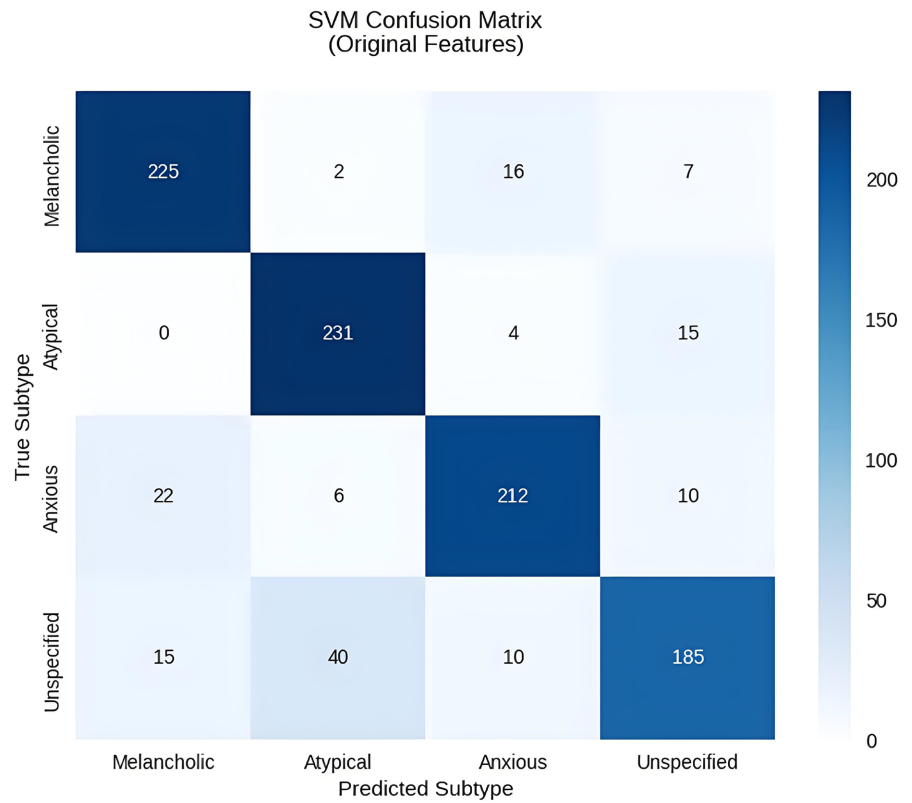


Figure 7. SVM confusion matrix using original features.

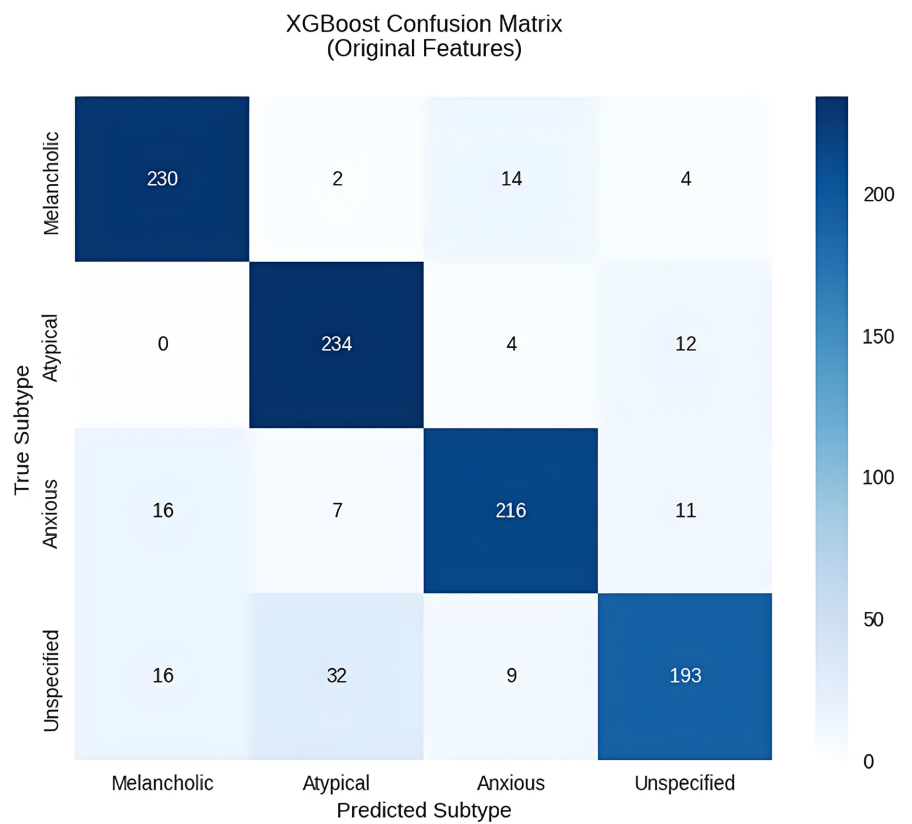


Figure 8. XGBoost confusion matrix using original features.

with 215 correct classifications, though minor confusion is observed with Melancholic (18) and Unspecified (11) predictions. The Unspecified category yields slightly more misclassification, particularly toward Atypical (39 cases), suggesting partial overlap in their feature distributions.

Figure 7 presents the confusion matrix for the Support Vector Machine (SVM) classifier trained on the original features. The model maintains competitive performance, accurately classifying 225 Melancholic, 231 Atypical, and 212 Anxious patients. Compared to Random Forest, SVM shows slightly more dispersion in predictions—particularly for Melancholic (16 misclassified as Anxious) and Unspecified (40 misclassified as Atypical). These results indicate SVM’s relatively softer margins, which can lead to more confusion in clinically ambiguous boundaries.

Figure 8 shows the confusion matrix for the XGBoost classifier, which demonstrates a strong and balanced performance. It achieves 230, 234, and 216 correct predictions for Melancholic, Atypical, and Anxious patients, respectively. Misclassifications are fewer than in the SVM model, especially for Unspecified cases, which are mostly confined within the true category (193 correct). The results suggest that XGBoost effectively captures nonlinear interactions in the feature space, improving subtype boundary recognition over margin-based approaches like SVM.

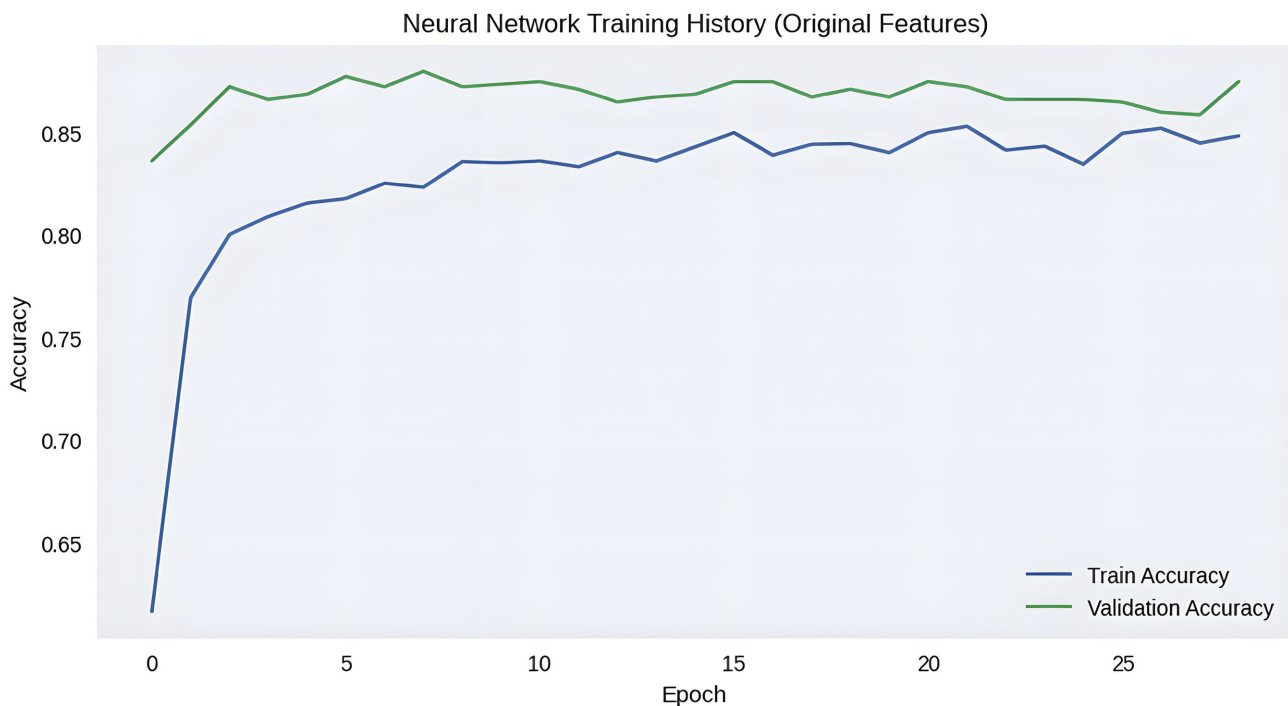


Figure 9. Neural network training accuracy across epochs.

Figure 9 presents the training history of the neural network classifier over 28 epochs, plotted as training and validation accuracy curves. The model shows rapid convergence within the first five epochs, achieving validation accuracy above 85% early in training. From epoch 6 onward, both curves stabilize, with no signs of overfitting or divergence. The consistent gap between train and validation curves

suggests well-calibrated generalization, likely due to regularization techniques such as dropout and batch normalization. These results reinforce the model's robustness despite the moderate complexity of the input feature space.

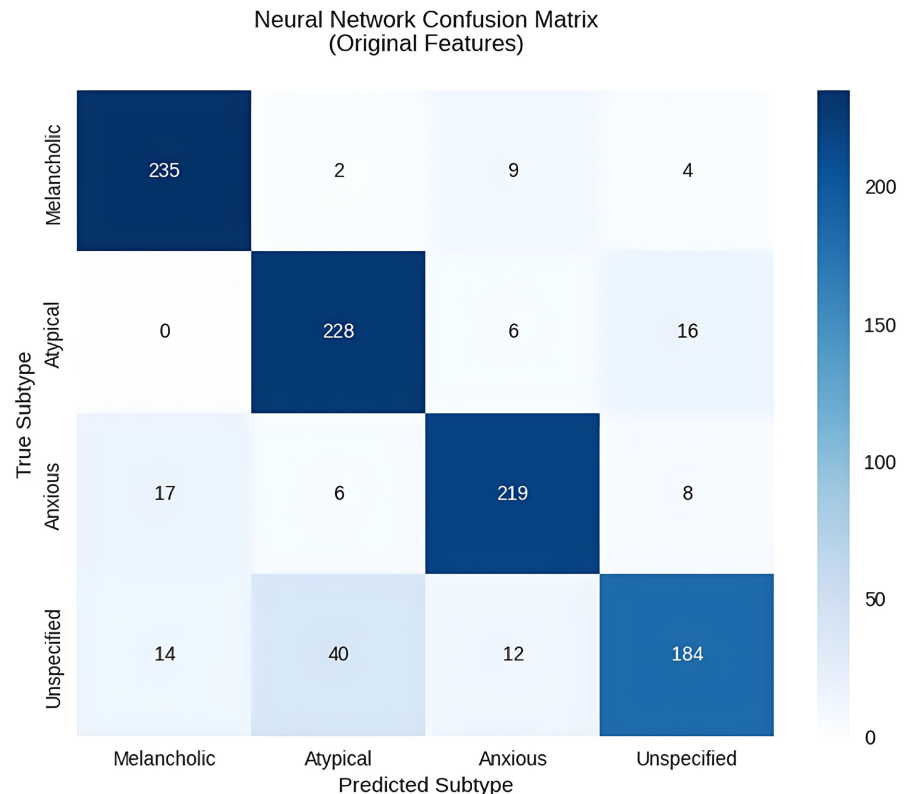


Figure 10. Neural network confusion matrix (original features).

Figure 10 illustrates the performance of the neural network classifier using the original clinical features, represented as a confusion matrix. The model demonstrates high classification accuracy for the melancholic and anxious subtypes, with 235 and 219 correct predictions respectively. The atypical group shows slightly more misclassification, particularly being confused with the unspecified subtype. The unspecified category also shows moderate overlap with the atypical class, highlighting a challenge in distinguishing borderline cases. Overall, the neural network performs competitively across all categories, with reasonably balanced sensitivity and specificity.

Figure 11 presents the confusion matrix for the Random Forest model trained on quantum-inspired features. The results show a substantial decline in classification performance compared to original features. The anxious subtype is particularly affected, with heavy misclassification into melancholic and atypical categories. The melancholic group shows reasonable retention (166 correct), but its misclassification into anxious and atypical categories signals a loss of discriminatory power. This suggests that while quantum-inspired transformations provide compact representations, they may also compress critical subtype-distinguishing variance needed for tree-based models.

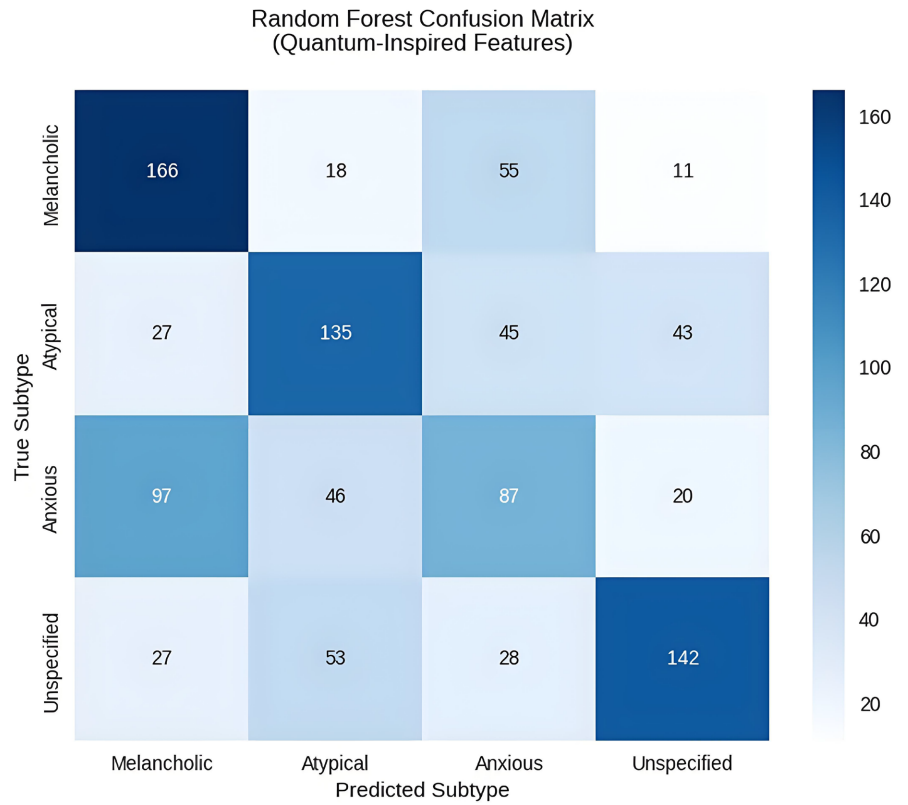


Figure 11. Random forest confusion matrix (quantum-inspired features).

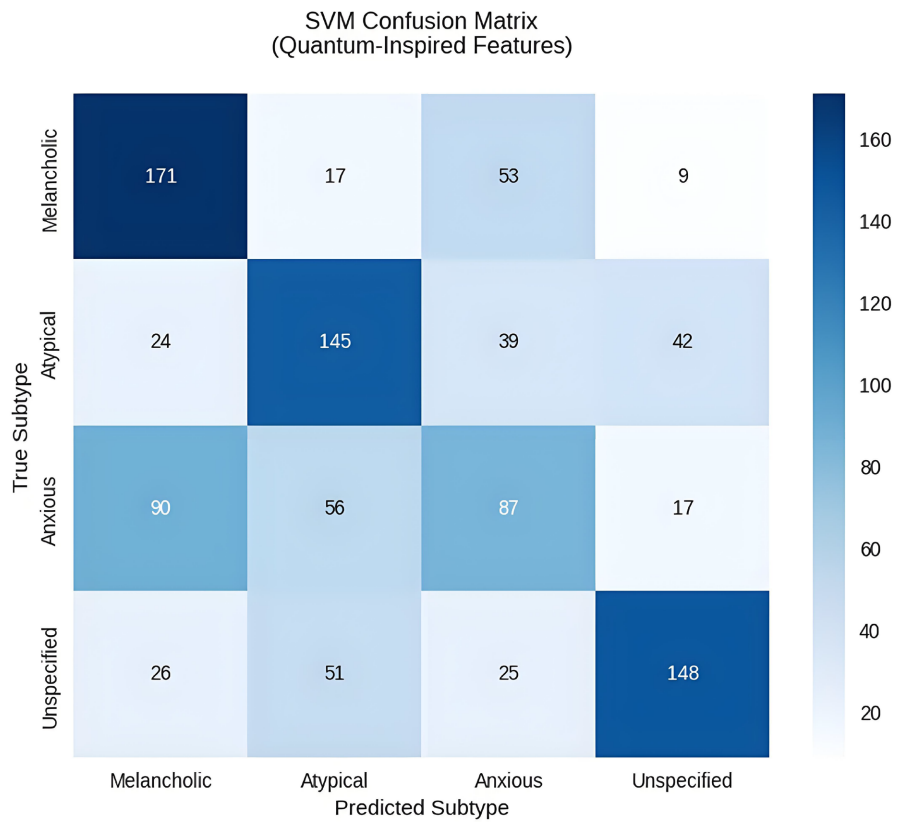


Figure 12. SVM confusion matrix (quantum-inspired features).

Figure 12 visualizes the confusion matrix for the Support Vector Machine (SVM) model using quantum-inspired features. Although the performance improves slightly compared to the Random Forest, significant confusion remains—especially for the anxious subtype, which is distributed across all categories. The melancholic class fares the best (171 correct predictions), followed by atypical. These results indicate that SVM is relatively more robust in handling abstract feature spaces than Random Forest but still struggles to achieve high-fidelity subtype classification using the quantum feature set.

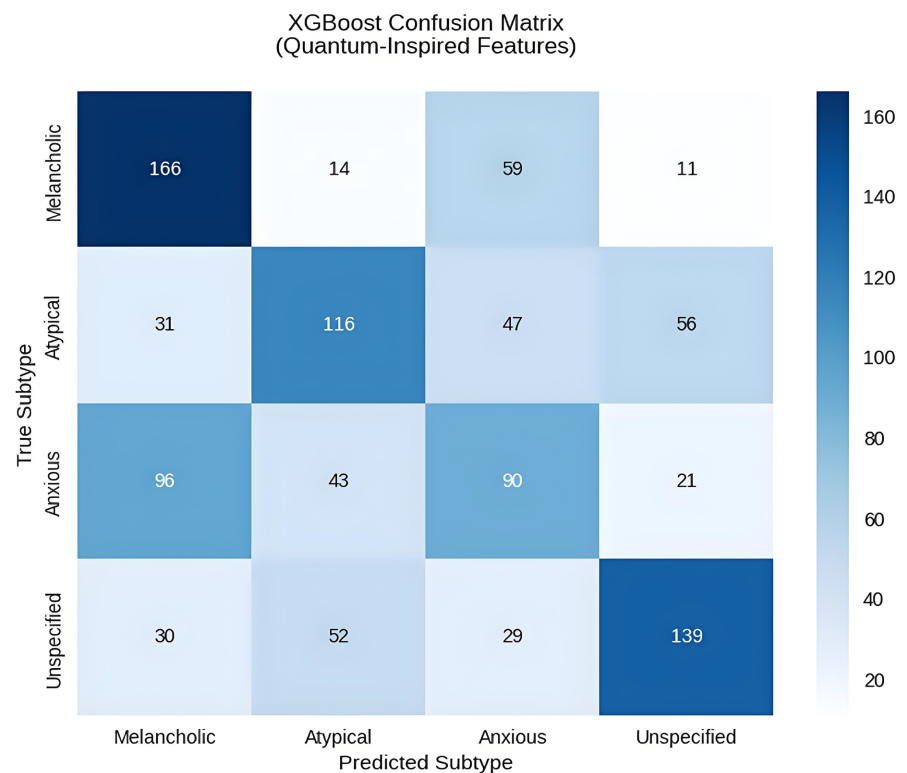


Figure 13. XGBoost confusion matrix (quantum-inspired features).

Figure 13 shows the XGBoost confusion matrix using quantum-inspired features. Compared to SVM and Random Forest, XGBoost exhibits a slightly more balanced classification, although accuracy levels are still lower than those achieved with original features. The melancholic and unspecified categories remain better classified, while the atypical and anxious subtypes continue to exhibit confusion, particularly with each other. The results indicate that boosting methods can partially recover some structure from the quantum-represented data but still fall short in separating complex clinical profiles.

Figure 14 depicts the training and validation accuracy curves for the neural network trained on quantum-inspired features. The learning trajectory shows rapid early convergence, with validation accuracy stabilizing around 55%, significantly lower than the original-feature model. The smaller gap between training and validation curves suggests good generalization but at the cost of underfitting due to lower-quality representations. This result further confirms that quantum-inspired

features, while innovative, may not fully capture the nuanced differences necessary for precise subtype prediction in this context.

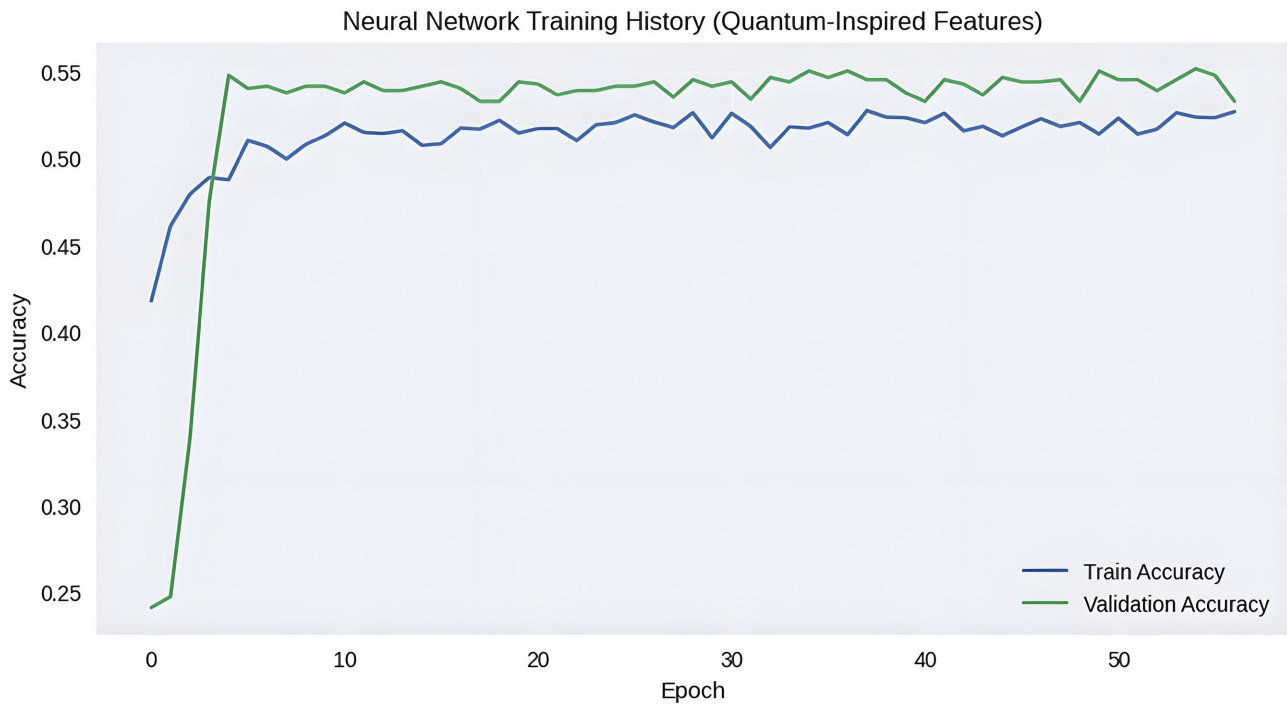


Figure 14. Neural network training history (quantum-inspired features).

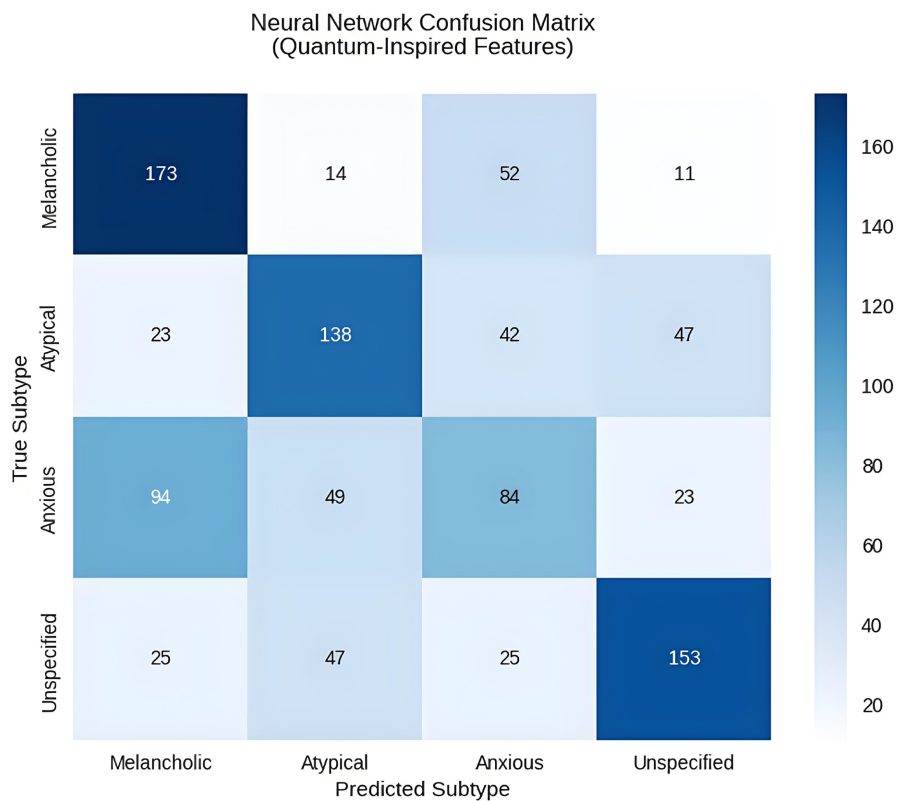


Figure 15. Neural network confusion matrix (quantum-inspired features).

Figure 15 displays the confusion matrix for the neural network classifier using quantum-inspired features. While the model captures general subtype patterns, performance is clearly diminished compared to the original feature set. The melancholic subtype maintains a relatively strong diagonal (173 correct predictions), but classification of the anxious subtype is notably poor, with widespread misclassification into melancholic (94) and atypical (49) categories. The unspecified subtype also shows moderate confusion with atypical. These results suggest that quantum-inspired transformations may obscure critical non-linear feature interactions needed by deep learning models to effectively separate clinical subtypes. Despite neural networks being theoretically well-suited to abstract feature spaces, their utility appears limited when fed quantum-inspired inputs lacking discriminative granularity.

6. Discussion

6.1. Interpretation of Findings

Although quantum-inspired feature mapping holds promise for encoding complex patterns in high-dimensional spaces, our findings suggest that classical clinical features still outperform quantum-transformed representations in predictive modelling. Across all classifiers, models trained on the original eight standardized clinical features demonstrated significantly higher accuracy, F1-scores, and ROC AUC values. One primary limitation of the quantum approach appears to stem from information loss during amplitude encoding, where continuous-valued clinical features are mapped to rotation angles and subsequently entangled into a compressed Hilbert space representation. This transformation can obscure clinically relevant variance especially when entanglement patterns are not explicitly optimized to reflect known relationships between features (e.g., cortisol-anxiety interactions). Moreover, dimensionality reduction may further dilute subtype-distinctive patterns. While quantum feature vectors initially exist in a 32-dimensional complex-valued space (derived from a 5-qubit circuit), any post-processing such as normalization or mapping to real-valued domains for classical model input may lead to additional abstraction that reduces clinical discriminability. The combination of non-domain-specific encoding and fixed gate architectures might hinder the emergence of separable clusters that are required for successful classification, particularly in nuanced diagnostic categories such as anxious or unspecified subtypes.

6.2. Clinical Relevance

From a translational standpoint, the ability to identify depression subtypes using model predictions is crucial for informing personalized treatment plans [52]-[55]. In this study, we explored subtype-specific treatment recommendations based on Random Forest predictions using quantum-inspired features. However, many predictions had posterior probabilities below 70%, indicating weak model certainty. Such low-confidence outputs are clinically problematic,

as they may lead to inappropriate interventions or delayed decisions. Furthermore, the confusion matrices (**Figures 10-15**) demonstrated pronounced misclassification for the anxious and unspecified subtypes both of which are frequently encountered in psychiatric practice and often require distinct therapeutic strategies. While quantum encoding introduces mathematical novelty, the lack of interpretable structure in the feature space limits its direct clinical utility [56]-[58]. Without clear mapping between quantum states and symptom patterns, it becomes difficult for clinicians to trust or validate the model's decisions. Until quantum encodings can retain interpretability, probabilistic certainty, and alignment with established clinical criteria (e.g., DSM-5), their integration into clinical decision support systems should be approached with caution [59] [60].

6.3. Methodological Limitations

Despite rigorous design, the current study has several notable limitations:

- **Synthetic Data Generation:** Although our simulated cohort was clinically informed, it lacks the noise, inconsistencies, and comorbidities inherent to real-world EHR or registry data. As a result, performance estimates may be optimistic and not generalize to clinical settings.
- **Static Quantum Circuits:** The feature mapping relied on fixed Ry-CX architectures with no learned parameters. More adaptive approaches (e.g., variational circuits or trainable gates) might better capture subtype-specific patterns.
- **Deterministic Statevectors:** All quantum transformations used deterministic statevector simulations. However, real quantum hardware introduces stochastic sampling effects, which could yield richer feature distributions or uncertainty measures that classical simulations fail to capture.
- **Lack of Hyperparameter Search for Quantum Encoding:** We did not perform optimization over qubit counts, gate layouts, or encoding orders. These may play a pivotal role in aligning the quantum feature space with the clinical decision boundaries.

6.4. Future Directions

To advance this line of research, we propose the following extensions:

- **Real-World Validation:** Apply the quantum feature pipeline to real-world clinical datasets, such as psychiatric EHRs or depression biobanks, to assess generalizability under real-world noise and missingness.
- **Variational and Hybrid Models:** Incorporate Variational Quantum Circuits (VQCs) or hybrid quantum-classical architectures, allowing the feature extractor to be partially learnable and better aligned with data distributions.
- **Quantum-Aware Feature Selection:** Develop preprocessing algorithms that identify which features are most amenable to amplitude encoding—possibly based on variance thresholds, mutual information, or graph-theoretic interdependencies.

- **Quantum Regularization for Neural Networks:** Design new loss penalties or constraints that promote robust learning from quantum features. This could include entanglement-aware dropout, gradient scaling for low-amplitude components, or customized learning rate schedules for quantum spaces.
- **Explainability and Visualization Tools:** Enhance interpretability by building tools that can back-project decisions from quantum feature space to original clinical input—akin to saliency maps or SHAP values in classical AI.

7. Conclusion

This study systematically investigated the potential of quantum-inspired feature transformations in the classification of clinically defined depression subtypes melancholic, atypical, anxious, and unspecified using a synthetically generated but clinically realistic dataset. By comparing the performance of four widely used machine learning classifiers (Random Forest, SVM, XGBoost, and Neural Networks) across both standard clinical features and quantum-transformed representations, we offer one of the first controlled benchmarks in this emerging application of Quantum Machine Learning (QML) in computational psychiatry. Our findings indicate that classical clinical features consistently outperform quantum-inspired features across all metrics, including accuracy, F1-score, and ROC AUC. While this result may seem discouraging from a quantum enhancement perspective, it reflects key limitations of current encoding strategies particularly the potential loss of domain-specific signal during amplitude encoding, the lack of adaptive circuit designs, and the deterministic nature of simulated quantum feature generation. Furthermore, the reduced classification certainty and interpretability observed with quantum-transformed data highlight critical barriers to clinical adoption. However, these limitations should not be interpreted as the failure of quantum machine learning in psychiatry, but rather as a call for further refinement. The framework developed in this study serves as a foundational testbed for future explorations. As quantum hardware continues to evolve and hybrid quantum-classical models become more feasible, several promising directions emerge incorporating variational quantum circuits, optimizing feature selection and encoding strategies, and developing explainable quantum AI tools that bridge the interpretability gap. Crucially, the integration of quantum-inspired techniques with real-world clinical datasets especially those from Electronic Health Records (EHRs), biobank repositories, or longitudinal psychiatric studies will be essential to validate utility, enhance generalization, and align with translational needs. Ultimately, while classical models remain superior in the current setting, the structured framework and insights presented here lay important groundwork for a future where quantum learning paradigms may complement or enhance psychiatric prediction and precision mental health care.

Conflicts of Interest

The authors declare no conflicts of interest.

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